THE UNIVERSITY OF QUEENSLAND

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Contemporary Angiography in the Diagnosis and Treatment of Cardiovascular Disease

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BSc (Hons)

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School of Medicine

Abstract

Background

Cardiovascular disease is the leading cause of death in the developed world. Angiography allows the visualisation of arteries through the use of real time X-ray imaging when injected with iodinated contrast media (ICM). Due to its excellent temporal resolution and real time imaging capability, angiography has been the cornerstone of the diagnosis and percutaneous treatment of cardiovascular disease for many years. The number and diversity of diagnostic and therapeutic procedures that utilise angiography are increasing rapidly but the technology of angiography is not without risk to patients and the staff in attendance. ICM used in angiography is excreted by the kidneys and is toxic. The cohort of patients being treated for cardiovascular disease are often elderly with pre-existing renal disease and more complex angiographic procedures can cause renal failure. There is also risk to the patient and the staff working in the room from the stochastic and deterministic effects of ionising radiation that is used to produce the images. Currently there is no multicentre reference levels for radiation dose to patients undergoing cardiac angiography procedures in Australia and globally there is little data on the factors impacting on staff dose during these procedures and the potential reductions available with newer X-ray systems. As new procedures, such as trans catheter aortic valve impanation (TAVI) emerge, there is a need to investigate the radiation doses associated with these, to investigate the impact of ICM on renal function and to assess new imaging techniques that may be useful for some of these newer procedures.

Methodology

Radiation benchmarks will be established for diagnostic and interventional procedures for Queensland public hospitals, with comparisons to the literature. With a single centre focus, radiation dose and procedural data will be collected to investigate the different variables that impact on radiation dose to the patient and the staff during diagnostic cardiac angiography and structural cardiac intervention. Further, the impact of latest generation X-ray equipment on radiation dose will be investigated during electrophysiology procedures, which are traditionally seen as high dose procedures. The impact of ICM usage and the effect on patient's renal function and mortality will be investigated during trans-catheter aortic valve implantation (TAVI). 3D angiography will be investigated to assess its

effectiveness, accuracy, ICM use and radiation dose compared to 2D angiography and computed tomography (CT) for patients undergoing TAVI. Finally, the degree of X-ray beam distortion, inherent in the design of all X-ray systems will be assessed for TAVI devices.

Results and conclusions

Radiation dose 75th percentile reference levels of 5864CGycm^2 and 12900CGycm^2 for diagnostic and interventional angiography procedures across all public hospitals in Queensland were established, which are very comparable to other international benchmarks. Radiation dose during diagnostic procedures is multifactorial but patient obesity was highlighted as the biggest predictor for both a high patient and staff radiation dose. During structural cardiac intervention the trans-oesophagel echocardiography operator had the highest radiation dose when compared to the rest of the team, but additional shielding was shown to reduce radiation dose by 82% and newer X-ray technology can dramatically reduce radiation dose, as demonstrated during electrophysiology procedures by up to 92%. ICM use was relatively high during TAVI procedures when compared to the literature but did not appear to be associated with acute kidney injury (AKI). The severity of AKI is important in determining mortality in these patients, which was linked to chronic kidney disease, respiratory failure, previous stroke, blood transfusion and retrieval or removal of the device, the latter being a new finding in this area. 3D rotational X-ray (DynaCT) can accurately determine the calibre and tortuosity of the ilio-femoral arteries, for patients selected for TAVI, using less ICM than CT but it was inadequate as assessing calcification in this particular study. The TAVI device was demonstrated to be significantly affected by X-ray beam distortion, when imaged toward the periphery of the image which could affect the implant depth.

Overall, cardiac angiography is evolving rapidly, with many new procedures utilising this technology. Radiation dose to patients and staff is now better understood, with new equipment and shielding technologies demonstrating dose reduction. The volume of ICM in these new procedures is not associated with AKI but pre-existing conditions are more relevant, as well as procedural complications. ICM volume can be reduced for these procedures through the use of new imaging technology, though it does have some limitations and TAVI devices can be susceptible to the effects of X-ray beam distortion.

Declaration by author

This thesis *is composed of my original work, and contains* no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including statistical assistance, survey design, data analysis, significant technical procedures, professional editorial advice, financial support and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my higher degree by research candidature and does not include a substantial part of work that has been submitted *to qualify for the award of any* other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

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Publications during candidature

Incorporated as Chapter 2:

J. Crowhurst, M. Whitby, D. Thiele, T. Halligan, A. Westerink, S. Crown, J. Milne. Radiation Dose In Coronary Angiography and Intervention: Initial Results From the Establishment of a Multi Centre Diagnostic Reference Level In Queensland Public Hospitals. *J. Med. Radiat. Sci.*, 2014 61 (3): 135–141

Incorporated as Chapter 3:

J. Crowhurst, M.Whitby, M.Savage, D.Murdoch, B.Robinson, E. Shaw, N. Gaikwad, R. Saireddy, Hay, K, Walters, D. Factors Contributing to Patient and Operator Dose During Diagnostic Cardiac Angiography. *J Med Radiat Sci.* 2019 66(1): 20-29 doi: 10.1002/jmrs.315

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J. Crowhurst, G.M. Scalia, M. Whitby, D. Murdoch, B.J. Robinson, A. Turner, L. Johnston, S. Margale, S. Natani, A. Clarke, D.J. Burstow, O.C. Raffel, D.L. Walters. Radiation Exposure of Operators Performing Transesophageal Echocardiography during Percutaneous Structural Cardiac Interventions. *J. Am. Coll. Cardiol*. 2018 71(11): 1246-54.

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J. Crowhurst, H. Haqqani, D. Wright, M. Whitby, A. Lee, J. Betts, R. Denman. Ultra-low radiation dose during electrophysiology procedures using optimized new generation fluoroscopy technology. *Pacing Clin Electrophysiol.* 2017 Aug;40(8): 947-954

Incorporated as Chapter 7:

J. Crowhurst, M. Savage, V. Subban, A. Incani, O. C. Raffel, K. Poon, D. Murdoch, R. Saireddy, A. Clarke, C. Aroney, N. Bett, D.L. Walters. Factors Contributing to Acute Kidney Injury and the Impact on Mortality in Patients Undergoing Trans-catheter Aortic Valve Replacement. *Heart Lung Circ*. 2016 Mar; 25(3): 282-9

Incorporated as Chapter 8:

J. Crowhurst, D. Campbell, O. Raffel, M. Whitby, P. Pathramanan, S. Redmond, A. Incani, K. Poon, C. James, C. Aroney, A. Clarke, D. Walters. Using DynaCT for the Assessment of Ilio-Femoral Arterial Calibre, Calcification and Tortuosity Index in Patients Selected For Trans-catheter Aortic Valve Replacement. *Int J Cardiovasc Imaging.* 2013, 29 (7): Page 1537-1545

Incorporated as Chapter 9:

J. Crowhurst, K. Poon, D. Murdoch, A. Incani, O.C. Raffel, A. Liddicoat, D. Walters. The Effect of X-ray Beam Distortion on the Edwards Sapien XT™ Trans-catheter Aortic Valve Replacement Prosthesis. *J Med. Radiat. Sci.*; 2015 62(4): 239-245

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Conference Abstracts:

Contrast Use and Acute Kidney injury in the elderly Patient Undergoing Intervention. J. Crowhurst, A. Incani, K. Poon, R. Shaffe, K. O'Keefe, C. Aroney, D. Walters *ASMMIRT 2013* – Tasmania (Oral)

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Contributions by others to the thesis

Incorporated as Chapter 2:

J. Crowhurst, M. Whitby, D. Thiele, T. Halligan, A. Westerink, S. Crown, J. Milne. Radiation Dose In Coronary Angiography and Intervention: Initial Results From the Establishment of a Multi Centre Diagnostic Reference Level In Queensland Public Hospitals. *J. Med. Radiat. Sci.*, 2014; 61(3), 135–141

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Substantial contribution to conception and design and analysis and interpretation of data. Critical review of paper for important intellectual content.

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Substantial contribution to conception and design. Critical review of paper for important intellectual content. Oversaw the project timeframes and logistics.

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J. Crowhurst, H. Haqqani, D. Wright, M. Whitby, A. Lee, J. Betts, R. Denman. Ultra-low radiation dose during electrophysiology procedures using optimized new generation fluoroscopy technology. *Pacing Clin Electrophysiol.* 2017 Aug;40(8):947-954

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J. Crowhurst, D. Campbell, O. Raffel, M. Whitby, P. Pathramanan, S. Redmond, A. Incani, K. Poon, C. James, C. Aroney, A. Clarke, D. Walters. Using DynaCT for the Assessment of Ilio-Femoral Arterial Calibre, Calcification and Tortuosity Index in Patients Selected For Trans-catheter Aortic Valve Replacement. *Int J Cardiovasc Imaging.* Volume 29, Issue 7 (2013), Page 1537-1545

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Angiography, Cardiology, Cardiovascular, Radiation dose, Contrast media, Acute kidney injury, Distortion, Computed tomography.

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Dedications

I dedicate this thesis to my family. To my wife Verena for her enduring support and to my children, Hannah, Danielle and Max who have missed out on valuable time with their father over the past six years, whilst I write, attend conferences and prepare presentations.

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List of Abbreviations used in the thesis

Abbreviation	Description
AF	Atrial fibrillation
AFA	Abdominal/femoral angiogram
AKI	Acute kidney injury
ANA	Anaesthetist
AVA	Aortic valve area
BIV	Bi-ventricular devices
BMI	Body mass index
CA	Coronary angiography
CAA	Complex atrial arrhythmia
CABG	Coronary artery bypass grafts
CAD	Coronary artery disease
CAD	Coronary artery disease
CCC	Concordance correlation coefficient
CCF	Congestive cardiac failure
CCL	Cardiac catheter laboratory
CKD	Chronic kidney disease
CIN	Contrast induced nephropathy
COPD	Chronic obstructive pulmonary disease
CORS	Coronary angiography
CORS-LHC/RHC	Coronary angiography + left heart cath + Right heart cath
CORS-LV/AO	Coronary angiography + aortogram/ left Ventriculogram
CORS-PA	Coronary angiography + pulmonary angiography
CT	Computed tomography

CVA	Cerebral vascular accident
CVD	Cardio-vascular disease
DA	Digital acqusitions
DAP	Dose area product
DRL	Diagnostic reference level
DYNACT	Dynamic computed tomography
EP	Electrophysiology
EPS	Electro-physiology studies
FOV	Field of view
FT	Fluoroscopy time
GFR	Glomelular Filtration Rate
GORD	gastro-oesophageal reflux disease
ICA	Invasive coronary angiography
ICD	Internal Cardiac defibrillator
ICM	Iodinated contrast media
ICRP	International committee of radiation protection
ICU	Intensive care unit
IDD	Instantly downloadable dosimeter
KAP	Kerma area product
K_{AR}	Kerma at the reference point
LADI	Left atrial device implant
LAO	Left anterior oblique
LBBB	Left bundle branch block
LOS	Length of stay
MRI	Magnetic resonance imaging
MSCT	Multi-slice computed tomography

MVI	Mitral valve intervention
MVI	Mitral valve intervention
NCRP	National committee of radiation protection
NYHA	New York heart association
OD	Operator dose
OP1	Primary operator
OP2	Secondary operator
PA	Pulmonary angiography
PA	Pulmonary angiography
PCI	Percutaneous coronary intervention
P_{KA}	Product kerma area
PPM	Permanent pacemaker
PPS	Pulses per second
PS	Procedural success
PT	Procedural time
PVD	Peripheral vascular disease
PVI	Pulmonary vein isolation
QA	Quality assurance
QH	Queensland health
RAO	Right anterior oblique
RAO	Right anterior oblique
RFA	Radio Frequency Ablation
RHC	Right heart catheterisation +/- venography
SID	Source image distance
STS	Society of thoracic surgeons
TAVI	Trans-catheter aortic valve implant

TAVI-WU	TAVI work-up
TAVI	Trans-catheter aortic valve replacement
TOE	Trans-oesophageal echocardiography
TOEOP	Trans-oesophageal echocardiography operator
TLD	Thermo-luminescent dosimeter
VAA	Ventricular arrhythmia ablation
VASI	Ventricular or atrial septal intervention

Introduction

In the context of this thesis, *cardiac angiography* is a generalised term used to describe an invasive procedure, using X-ray fluoroscopy, to image the heart chambers and its arteries, take measurements of blood pressure, oxygen saturations and electrical activity. As an adjunct to cardiac angiography, percutaneous treatments of various pathologies can be performed and specialised devices can be implanted to aid such treatment, the term *cardiac intervention* is a generalised term, used in this thesis to describe these procedures.

The first cardiac catheterisation was performed by Werner Forssmann, who in 1929, inserted a catheter from the arm into the heart and recorded this on X-ray film. Later he injected contrast media to demonstrate that the chambers of the heart could be imaged with fluoroscopy.(1) These basic elements of angiography remain today, almost 90 years later, but in the modern era, cardiac angiography procedures have matured. Cardiac catheterisation laboratories have been designed for the sole purpose of imaging the heart. New procedures are being developed at a rapid rate, and the procedures are also becoming longer with increasing complexity.(2) Where devices once only consisted of internal cardiac pacemakers and coronary stents, now heart valves can be replaced(3) and repaired(4), septal defects can be plugged and the left atrial appendage can be occluded,(5) all via percutaneous access under fluoroscopic control. These new advances mean that procedures are increasing in number and some are associated with higher radiation doses.(2) Radiation doses from cardiac angiography and cardiac intervention are relatively high.(6) The high radiation doses from the X-rays have risks to the patient and the staff working this environment.(7) There is the stochastic risk of malignancy and also the deterministic risk of skin injury.(2) The stochastic risk is difficult to quantify but increases with radiation dose and the relationship between radiation dose and stochastic effect is not known.(7) The deterministic effects by way of skin lesions induced by radiation are better understood and reports of skin injury from fluoroscopy X-rays have been reported many times in the literature.(2,8-12) In addition, the iodinated contrast media (ICM) used for many of these procedures to visualise heart chambers and arteries can adversely affect renal function, termed contrast induced nephropathy (CIN),(13) as ICM causes cellular injury and death to renal tubular cells (14).

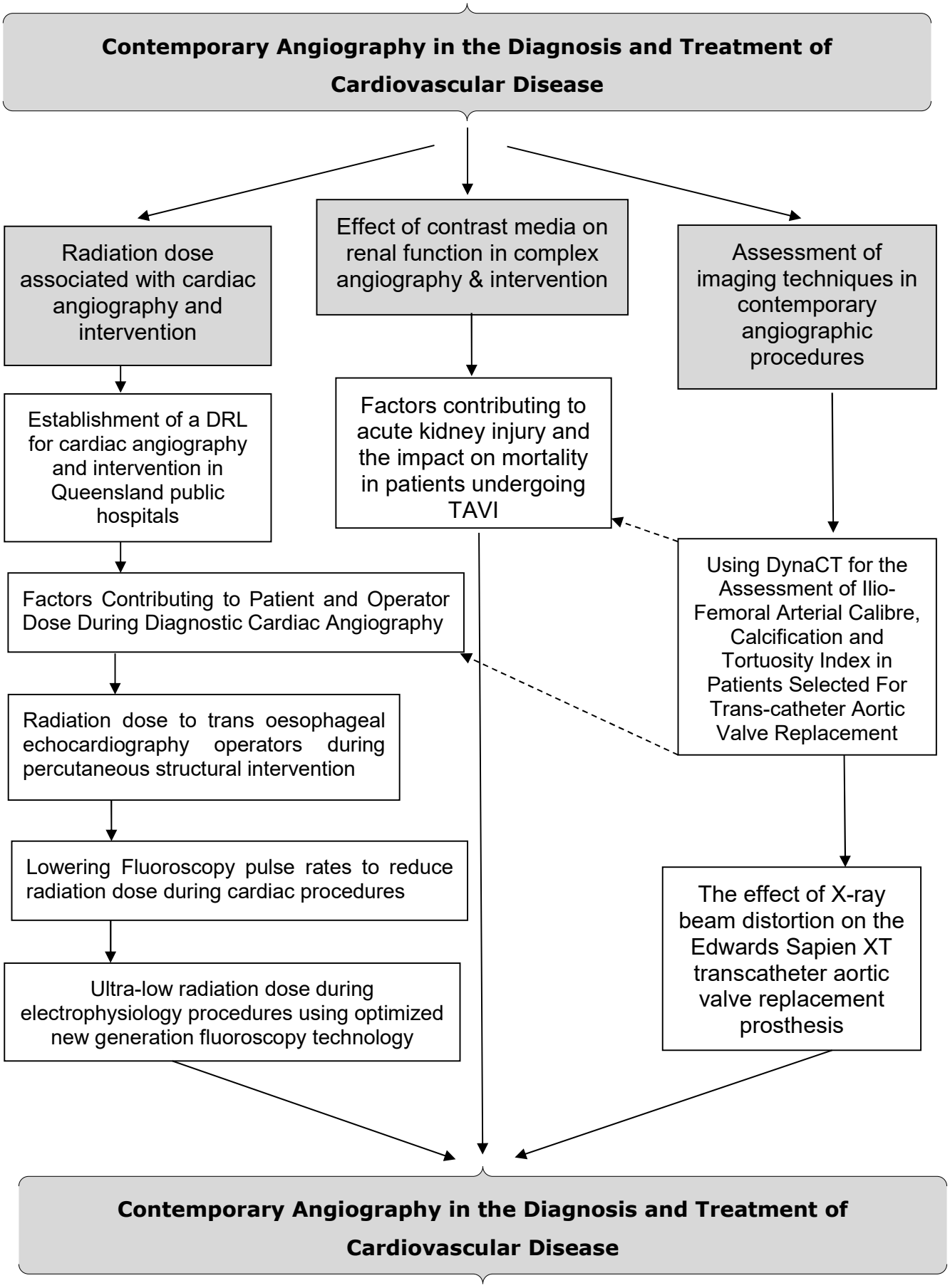
Objectives:

From a radiographer's perspective, working in this field, there are three main elements to cardiac angiography that warrant investigation as part of this thesis.

1. Radiation dose to the patient and the staff present for these procedures; what are the dose levels, what impacts on the dose and how can it be reduced?
2. Given the high-risk cohort of patients undergoing transcatheter aortic valve implantation (TAVI), what contrast media volume is used and what are the levels of acute kidney injury? What is the impact of this on patient outcome?
3. Can new advances in fluoroscopic imaging technology, such as rotational angiography demonstrate the anatomy and pathology relevant for these newer procedures and do the basic principles of fluoroscopic beam distortion have an impact on the TAVI device?

The overarching structure of this thesis and how these objectives have been addressed is outlined in the following research diagram.

Research flow diagram



Chapter 1 - Background and literature review:

1.1 Radiation levels in the cardiac catheterisation laboratory

Establishing acceptable radiation dose levels that X-ray units use to perform procedures is an important step in radiation dose management and is recommended by the International Committee for Radiation Protection (ICRP)(7). Comparing radiation levels to benchmarked levels or diagnostic reference levels (DRLs) is important and they are used a guide as to what radiation dose should be achievable for a particular imaging procedure using X-rays.(7) The recognised radiation values for comparison are the dose area product (DAP) (Kerma area product (KAP)), the skin entrance dose (or air Kerma) and fluoroscopy time.(7) DAP (KAP) is generally used, as it measures both the radiation exposure and the area exposed and is the unit that was used to aid comparison in the large UK series.(15,16) In addition, fluoro time has been described as a less reliable indicator of patient skin dose than DAP or $K_{ar,}$ as described in one recent study.(17)

Diagnostic reference levels have been investigated many times by national bodies around the world. The UK series was the first, and have been collecting data since 1992. In 2000 they reported a dose of 25.8 (22.3-36.3) $Gycm^2$ for coronary angiography,(15) which was lowered to a dose of 23.5 $Gycm^2$ (18.9-29.0) by 2005 (18) but was similar in 2010 (23 (16-31) $Gycm^2$).(16) These results demonstrate the importance of DRL studies and that once the median and 75^{th} percentiles are established, efforts can then be made to reduce dose. Other studies published from Europe, such as the study by Samara et al quoted a DAP of 45 $Gycm^2$ for CA and 90 $Gycm^2$ for percutaneous coronary interventional procedures (PCI) in Swiss academic hospitals.(19) However, one of the largest DRL studies, in terms of area covered was that published by Neofotistou et al in 2003, which examined doses from six European countries for CA and PCI and established 75^{th} percentile values of 57 and 94 $Gycm^2$ respectively.(20) D'helft et al published a median value of 31 Gycm2 in 2009 for CA procedures across 19 individual X-ray apparatus in Ireland.(21) The United States published median values of 49 $Gycm^2$ for CA and 83 $Gycm^2$ for PCI procedures in the publication by Miller et al in 2012 as advisory data sets (22) and Greece performed a large DRL study across 26 centres, published in 2013 by Simantirakis et al, suggesting a median and 75^{th} percentile DRL of 37.5 Gycm2 and 53 Gycm2 respectively for CA.(23) More recently, a study has been published by Ngaile et al in 2018, with a DRL for Tanzania, with median values for CA of 37.8 Gycm2 for CA and 86.5 for PCI, though the sample sizes from the two major hospitals involved were relatively small.(17)

As at 2013, there were no DRL values for CA and PCI in Australia. It is not clear why a DRL study has not been performed in Australia before. It is surprising, given that so many western countries had achieved this in the early 2000's. Without measuring radiation doses from multiple sites and establishing a benchmark, there is no way of knowing whether doses used by cardiac catheter laboratories (CCLs) in Australia are overly high or even low when compared to the rest of the world.

It is clear when reviewing the literature that there is a large variation in median doses for these procedures. There would undoubtedly be equipment, protocol and procedural differences between the countries and some studies have normalised their doses to a median patient weight, such as that by Hart et al in the UK DRL series,(16) which adds a further level of confusion, when comparing data. This is in line with a paper by Chapple et al who normalized radiation dose to an average of 70Kg(24). Normalising the dose to a particular patient weight is advantageous for a comparison between x-ray systems. Normalising the dose data to a reference patient weight is difficult with a large number of facilities. Many multi-centre studies have not elected to do this. (20,22,25,26) A higher DAP value than some of the literature may be the result, due to a higher or lower median patient weight. Another method utilised to normalise the DAP data is to exclude patients outside a weight range of 80Kg ± 5, with the same aim(18). Normalizing may not be logical in establishing a DRL for practical routine use, as the DRL would only be relevant to a small portion of patients that fall within a certain weight range. The ICRP published guidelines for the creation of DRLs in 2017 and advise that it is difficult to implement DRLs for interventional procedures given the wide range of patient size and other factors such as procedural complexity but that influence the DAP. However, it does suggest that the DRL process should be applied in the same manner as for diagnostic procedures. Dose data can be normalized to patient body habitus but similar results can be obtained without normalization.(27)

Given the variation, it is reasonable that DRLs should be established at the local level and that each facility dose be audited and compared to the DRL on an annual basis, as suggested by the ICRP.(7) Therefore, the first objective for the author of this thesis was to establish a benchmark (DRL) for the most commonly formed cardiac angiography procedures; diagnostic coronary angiography and precutaneous coronary intervention. Once radiation doses are established, efforts can be made to reduce the radiation dose required for these procedures, which will undoubtedly lead to a lower risk of the stochastic

and deterministic effects of radiation. This is the trend that has been seen in the UK series by Hart et al.(28)

1.2 Factors that impact on radiation dose in the cardiac catheterisation laboratory.

X-ray system imaging protocol

It stands to reason that the dose output of the X-ray system will impact on patient radiation dose. One of the most readily achievable methods of dose reduction is that of changing the settings of the X-ray system. A lower pulse rate is a simple method that can reduce radiation dose in the cardiac cath lab when performing coronary angiography. On this topic, Abdelaal et al reduced fluoroscopy pulse rate from 15 pps to 7.5 pps in a randomised controlled trial. A DAP reduction of 26% was achieved and an operator dose reduction of 40% was also achieved.(29) In a small study of 39 patients, Ebrahimi et al demonstrated that lowering the fluoroscopy and cine frame rate from 15 fps to 7.5 fps, without any other changes reduced the radiation dose to the patient from 433 to 252 mGy for CA procedures, without adversely impacting on image quality.(30) Another study that adjusted the fluoroscopy pulse rate and the X-ray system dose protocol was that by Wassef et al in 2014. They implemented system changes to the X-ray machine in addition to other parameters. They also, in a sub group analysis, reduced the cine frame rate from 15 to 7.5 frames per second. A 35% reduction was seen in the system reduction group and a 65% reduction was seen in the lower frame rate reduction group.(31) A further study by Maccagni et al, published in 2017 investigated the impact of lower pulse rates during PCI and reduced radiation dose with their low dose protocol from 115 $Gycm^2$ to 53.3 $Gycm^2$.(32) Importantly, in this cohort of patients, where doses are higher than for CA, the percentage of patients that exceeded the 5Gy reporting threshold were significantly lower; 1.8% vs 7.2% with the low dose protocol.(32) These papers demonstrate that traditionally used frame rates can be reduced to significantly reduce radiation dose without overtly impacting on image quality. Badawy et al reduced their fluoroscopy pulse rates to 3 pulses per second in an effort to reduce dose. Their paper also described the changes that were made to the X-ray system in an effort to improve image quality at this low pulse rate. Their dose reduction was impressive and the 3 pulse per second fluoroscopy is the lowest recorded for coronary angiography in the literature. (33)

X-ray equipment dose reduction technology

When radiation doses are reduced during fluoroscopy, image quality can suffer and a low dose image will appear grainy or *noisy*.(2) Noise reduction software with new X-ray technology, allowing a lower radiation dose to be used has featured for both coronary angiography procedures and electrophysiology procedures. Bracken et al demonstrated in

268 patients in 2015 how the Philips Allura Clarity (Brest, Netherlands) system reduced DAP by 46% when compared to a similar system without the noise reduction technology.(34) Eloot et al published a very similar study, also in 2015 on 70 patients, comparing the Philips Allura Clarity to the Philips Allura FD10 but this time, found that the Allura Clarity system reduced dose by 75%.(35) A further study by Christopoulos et al compared four currently available X-ray systems and compared the dose outputs with a phantom. There was a significant difference between the four systems, and again the Philips Allura Clarity demonstrated the lowest DAP and film dose.(36) There are other novel ways to reduce dose: Kuon et al described the use of electrocardiogram (ECG) gated fluoroscopy and cine in 2015, with a Siemens X-ray system, as an additional method of reducing radiation dose, describing it as 'feasible in clinical routine' and it 'tremendously minimises patient radiation exposure', though it unfortunately was not compared to the same system when not utilising the ECG gating as a comparison.(37) Its use does not appear to have been investigated further in the literature. Didier et al investigated the impact of a dose reduction strategy with a new X-ray system, (GE IGS 520) in a study in 2016. They demonstrated how a number of new dose reduction features, including reducing the fluoroscopy pulse rate, could reduce DAP for CA and PCI procedures. However, they did note that patient BMI did have a large impact on DAP during procedures. They also noted that radial access was associated with more DAP, longer cine time and fluoroscopy time.(38)

Removal of the stationary grid

The stationary grid used in X-ray systems reduces scattered photons reaching the detector and improves image quality.(39) Removing the stationary grid may reduce image quality but it should also reduce patient dose. Removing the stationary grid from the housing of the detector/image intensifier was first documented by Partridge et al in 2006, and instead used an air gap technique to reduce scatter and image noise. Similar image quality was obtained for an approximately 50% dose reduction during CA.(39) Roy et al also removed the anti-scatter grid for patients with a BMI of less than 25 kg/m^2 in a series of 129 patients. They too found that removing the grid did not adversely impact on image quality in their lower BMI cohort and that radiation dose was reduced by 47%. Also, during phantom studies, operator dose was reduced by over 50% in all projections.(40)

Arterial access route

Radial artery access is now preferred for CA and PCI as it has lower complication rates and is preferred by patients as communicated in a publication by Archbold et al in 2004.

(41) Jolly et al also demonstrated lower rates of vascular complications in the RIVAL trial in 2011 which enrolled 7021 patients from 158 centres and 32 countries. It also demonstrated lower rates of death, myocardial infarction, stroke and bleeding which was the composite endpoint.(42)

These papers highlight the attractiveness of the radial artery access route. Radial access has however, been demonstrated many times to be associated with a higher radiation dose for the patient than for femoral access. In 2008 Brasselet et al studied radiation dose the patient and operator. For the patient, radial access was associated with 65.8% higher dose for CA and 28.2% higher for CA with ad hoc PCI. Operator dose was also higher.(43) A randomised trial by Brueck et al in 2009 of over 1000 patients for CA and PCI demonstrated that longer fluoroscopy times and higher DAP was associated with the radial approach. There were however fewer vascular complications in the radial group.(44) In 2016 Shah et al also studied left vs right radial and femoral approach. Whilst there was not a significant difference between left and right radial access, there was a significant difference between radial and femoral access for DAP, AK, fluoroscopy time and operator dose.(45) A further randomised controlled trial was performed by Michael et al in 2015. It included 128 eligible studied patients undergoing angiography who had had previous bypass surgery. In that study, fluoroscopy time was higher for radial approach, as was contrast media use, though air Kerma was not significantly higher. Operator dose on the other hand was significantly higher with the radial access.(46)

The REVERE trial by Pancholy et al in 2015 randomised patients to left radial, right radial and right femoral approach, with almost 500 patients in each arm. They found no significant difference in radiation dose between the access routes but did note that operator experience was significantly associated with radiation exposure (air Kerma), with the least experienced operators delivering the most radiation.(47) In 2016, Singh et al demonstrated a significant difference between radial and femoral access in a study investigating operators under training. They found radial access was associated with higher fluoroscopy times and DAP and also that procedure time reduced during years of training, though DAP did not significantly decrease.(48) Also in 2016, Simard et al, demonstrated a 15% higher radiation dose associated with radial access in a study with data spanning 10 years from 6 countries and 10 different centres. This study concluded that as the numbers of radial and femoral access procedures in a centre became equivalent, DAP values became equal, demonstrating a learning curve with the technique.(49) In addition, Gray et al found no difference in DAP with radial access

compared to femoral access in a high volume centre.(50) In 2017, a French national multicentre study by Georges et al found lower doses with radial access (RAY'ACT-1) with over 55,000 patients in the cohort. It also demonstrated that in centres where both radial and femoral access routes were used, doses were lower with femoral access compared to radial for CA and PCI and that dose was related to the rate of radial vs femoral access.(51) However, one study by Norgaz et al in 2012 found that left radial access was associated with less fluoroscopy time than right radial access in a randomised trial of 1000 patients, though DAP was not significantly different.(52)

Patient factors

Patient obesity was demonstrated to impact on radiation dose in 2007, in an abstract at the Cardiac Society of Australia and New Zealand (CSANZ) annual scientific meeting. That study found that obese patients had a significantly greater DAP than normal weight patients.(53) Shah et al performed a similar study, published in 2015, with 3750 patients and demonstrated how obese patients record a DAP 2.5 times greater than normal weight patients and patients with a BMI >40 kg/m^2 receive a DAP that is four times greater than normal weight patients.(54) BMI therefore has a large impact on a patients' radiation dose.

Biplane angiography

The use of biplane angiography and the impact on radiation dose has not been reported that many times in the literature. Biplane angiography offers the benefit to the patient of taking 2 cine acquisitions for a single contrast media injection, thus reducing contrast load. This aspect is of interest because at the authors centre, both cardiac angiography suites are of the biplane type. Sadick et al investigated the use of Biplane imaging for PCI procedures and demonstrated a 36% higher DAP for biplane procedures than single plane. Surprisingly, there was no significant difference in contrast load between biplane and single plane procedures. (55) Lin et al investigated radiation doses during diagnostic biplane procedures and found that radiation doses were 17% higher for biplane than single plane and were significantly higher for all variables studied.(56) Smith et al investigated biplane imaging for coronary angiography in 2018, using multivariate analysis in 5176 patients, the largest cohort to date. Their findings indicated that there was a 28% reduction in contrast media, at the expense of a 23% increase in radiation dose.(57) These studies suggest that biplane imaging has a significant impact on radiation dose but to the author's knowledge, there is no data on the impact of biplane imaging on operator dose.

Operator experience

Education of staff, particularly the primary catheter operator is another important factor to consider. In 2009 Georges et al investigated the effect of a two day education course on DAP during CA and PCI procedures in addition to equipment protocol changes and reducing the number of ventriculograms. They reported a 50% reduction in DAP after the course and the changes in protocols. Interestingly, the lowest doses were seen in the three months immediately after the course, with a rebound effect seen after time that and doses increased again.(58) This would indicate that there is possibly a need for ongoing education and at least an annual refresher would be necessary, as is the current status in Queensland hospitals.

Staff member operating the equipment

Some cardiac catheterisation laboratories have the cardiologist operating the X-ray equipment and some employ a radiographer to operate this aspect of the angiography procedure. There is limited literature as to the most effective method of working, however one study by Arthur et al, published in 2002 found that there was no difference in the fluoroscopy times and dose whether cardiologists or radiographers controlled the exposure but there was less during digital acquisition mode when the cardiologist was controlling its operation.(59)

Multiple factors

Christakopoulos et al measured a multitude of factors predicting radiation dose in 748 CTO procedures across 9 US centres in 2017. They found that a higher BMI, prior coronary bypass surgery, calcification and long occlusion length were predictors of high radiation dose under univariate and multivariate analysis. This is important, as CTO procedures are associated with long fluoroscopy times and radiation doses. Median air Kerma in this study was high: 3.4 Gy.(60) Understanding which factors predict higher doses during cardiac angiography is of utmost importance, and this study highlights some of the factors that can impact on this.

1.3 Occupational radiation dose for the catheter operator

Staff who perform cardiac angiography and intervention are also exposed to radiation in the cardiac catheter laboratory. This includes the primary operator who inserts and manipulates catheters in the heart, their assistant and other staff that are present with the procedures. The number of staff required for these procedures may also increase as the complexity increases. Considering the length of time that many may work in this environment, recording their exposure and reducing their exposure are important considerations. In addition their radiation dose needs to be kept within acceptable limits.(7)

With regard to staff radiation dose; the concerning series of papers by Roguin et al investigating brain and neck tumours amongst interventional physicians using fluoroscopy(61-63) found that left sided tumours were more likely than right sided tumours,(63) which is important as most of the time, the operator's left side faces the radiation and the associated backscatter. Whilst the radiation was not established as the source of the malignancy, it is a significant body of work that raises awareness of the risks of radiation to personnel working in this field. Attributing the risks of occupational radiation to an increased risk in cancer in the modern era is difficult, though the study by Andreassi et al in 2016 did demonstrate this. Using a structured questionnaire at a Cardiology conference in Italy, delegates answered a series of questions on their health status and health history, and they were grouped as either cath lab workers or non cath lab workers, which was the control group. The study found that cath lab workers were at a higher risk of skin lesions, cataracts, depression, orthopaedic problems and thyroid disease in comparison to the control group. There was also an increase in the risk of skin lesions, hypertension, hypercholesterolemia and importantly cancer across years of working.(64) This important paper highlights the risks to those working with radiation in comparison to those who do not.

Radiation is generally understood to be a linear, no-threshold relationship to cancer, meaning that as the amount of exposure increases, the risk of cancer also increases, though the severity of the cancer is not related.(7) As a result, it is recommended by the ICRP that all personnel that work in a cath lab should be monitored with calibrated dosimeters that are read on a regular basis. High radiation dose should then be investigated if it occurs.(7) The problem that this type of monitoring has is that it does not highlight when the high dose was received, and whether it was an false reading after leaving the dosimeter in the cath lab for a period of time instead of in the correct storage

location or whether the high dose was genuine and was attributed to when the staff member was working in the cath lab. Measuring radiation on a case by case basis has the advantage of highlighting where and when higher than usual radiation doses were received. However, most of the reported literature relate to small prospective studies investigating the effect of only one particular variable. For instance, one of the earliest papers investigating access route and operator dose was by Brasselet et al in 2008, when they studied radiation dose to the patient and operator during radial and femoral artery access routes. In 420 procedures, the patient dose for radial artery access was associated with a 65.8% higher dose for CA and 28.2% higher for CA with ad hoc PCI than femoral artery access. Operator dose, however, was the primary outcome of this study and was determined with two electronic dosimeters. Patients were heavier in the radial group, 80 vs 76 Kg, which could have contributed to the higher doses. Radial dose for CA was 29 μSv for radial and 13 μSv for femoral artery access. They did comment on how operator dose was 'strikingly related' to patient exposure (r=0.68 for radial and r=0.62 for femoral CA). They also commented that there were other variables that were related, such as procedure duration and fluoroscopy time and that BMI was related to DAP but surprisingly not operator dose.(43) This is one of many studies investigating arterial access location and the impact on radiation dose to the operator.

Effective dose

Staff dose is measured using calibrated dosimeters. For an interventionalist this should be between 2 and 4mSv per year.(7) Effective dose is derived from the calculation of dose to each specific organ.(7) Different organs have different tissue weighting factors, meaning that certain organs are more sensitive to radiation than others. The breasts, colon, lung, stomach and bone marrow are particularly sensitive.(65) However, Brain tumours appear to be of particular concern.(63,65) In addition, the lens of the eye is also of concern, cataracts can form and are seen in up to 50% of interventional cardiologists.(65)

Impact of arterial access route

Dominici et al investigated radiation exposure to the operator in 2013 when comparing left versus right radial approach, in a randomised controlled trial of 413 patients. They discovered that even though there was no difference in DAP between the two arms, operator dose was significantly lower with the left radial approach. Average operator radiation dose was 33 and 44 μSv for left and right radial approach respectively.(66)

In a further randomised controlled trial, in 2015, Michael et al studied 128 eligible patients who underwent angiography and who had had previous bypass surgery. In that study contrast media volume was the primary endpoint and radiation dose to the patient and operator was a secondary endpoint. Contrast media volume was higher for radial access and fluoroscopy time was higher for radial approach, though air Kerma was not significantly higher. There were two operators for each procedure, operator one received 26, mrem for radial access and 1.3 mrem for femoral access. The second operator was also significantly higher, 18 vs 0.8 mrem.(46)

In the REVERE trial, Pancholy et al, randomised patients to left radial, right radial and right femoral approach, with almost 500 patients in each arm. They obtained a different result for this situation from Dominici et al and found that the left radial approach was associated with a significantly higher operator dose than the other access routes. In addition, the less experienced operators demonstrated a higher operator dose, highlighting the impact that operator experience has on radiation dose to operator. This study used the Instadose^{TM} instantly downloadable dosimeter.(47)

A sub-arm of the MATRIX trial, (which investigated bleeding in radial vs femoral approach PCI during acute myocardial infarction) was the RAD-MATRIX study, published in 2017, where operators wore dosimeters when patients were randomised to either radial or femoral approach. There were 777 patients, intervened on by 18 operators. DAP was the same in both groups but thorax dose was significantly higher in the radial group. Calculated effective dose was also higher: 2.3 vs 1.2 uSv. Thorax dose was also significantly higher when normalised to DAP. A sub group analysis investigating left vs right radial access found that operator effective dose was higher with right radial access but was non-significant when normalised to DAP.(67)

The RAD-MATRIX results are confirmed by the RADIO study (Kallinikou et al 2016) in which 830 patients undergoing CA with PCI were performed either radial or femoral. They found that right radial and left radial procedures delivered a higher dose to the operator when normalised to DAP than the femoral approach. Right radial dose was higher than left radial. Interestingly in this study, additional radiation protection was used, by means of a lead equivalent drape around the access site.(68)

Shielding solutions for staff

Staff that work in the cath lab need to be protected from the occupational backscattered radiation dose. Staff should wear a lead or lead equivalent apron that covers the torso and

the primary operator should wear a lead thyroid collar and lead glasses.(69) Standard shielding solutions in cath labs consist of a lead drape hanging from the table side and a ceiling suspended lead acrylic shield.(2) The effectiveness of the ceiling suspended shield has been documented recently: In 2017 Jia et al used real time dosimeters, a phantom patient and manikins to measure the effectiveness of the radiation shield and concluded that the ceiling suspended shield reduces radiation dose to the primary operator by up to 90%. In addition, they demonstrated that LAO projections produced more radiation dose for the operator and that having the ceiling suspended shield close to the operator gave the best protection.(70) Even though this study appears simplistic, it is important as it demonstrates both the effectiveness of the shield and where best to position it to be as effective as possible, with the shield giving the best protection when closest to the operator. In 2015, Eder et al demonstrated that changing the design of the lead acrylic shield can reduce radiation dose if strips of lead are attached to the lower edge of a slightly larger shield. Dose to the operator can be reduced further if lead drapes are placed on the patient.(71)

Given that generally, radial access has been associated with higher radiation doses to the operator, additional shielding devices have been developed to counter this trend. In 2010 Behan et al designed a special radial arm support with inbuilt radiation protection by way of a vertical 20cm high piece of polycarbonate, with a sheet of 0.5mm lead rubber glued to it. In 106 patients, this simple device reduced radiation dose from 19 to 12 μSv for diagnostic CA and 61 to 23 μSv for elective PCI, without changing any other factors and with a similar DAP in each group.(72)

In 2012, Ertel et al investigated different shapes of lead protection that were placed on the phantom patient under controlled conditions. All lead drapes gave the same 0.28mm of lead equivalency and they found that all shapes of lead drape significantly reduced the radiation to the operator. The L shaped device gave the greatest protection to the operator, reducing the dose to the operator by 72% in comparison to the other shaped drapes that gave 65% and 58% respectively.(73) In addition, Liu et al demonstrated in 2014 that when optimal radiation protection was in place, radial access gave a lower torso radiation dose to the operator than femoral access under a phantom simulation. They did find, however, that the hand dose of the operator was higher with radial than with femoral access.(74)

Also in 2012, Lange et al performed a small single centre study on 305 patients and demonstrated again that radial access operator dose was higher than femoral access dose

when no additional shielding was in place. However, they demonstrated that with shielding in place, by way of a pelvic drape, DAP normalised dose was reduced by the same amount in each group, concluding that even with shielding in place, radial access gave a higher operator dose than femoral access.(75)

Musallam et al demonstrated a threefold reduction in radiation dose to the operator with pelvic shielding on the patient in a randomised controlled trial. The study was published in 2014 and enrolled 322 patients. They demonstrated that with a sheet of lead rubber placed on the patient's pelvis and thighs, operator dose was reduced significantly. However, radiation to the patient, as measured beneath the apron was twice as high. The authors concluded that the use of pelvic shielding should be further investigated before being adopted widely.(76)

Other than shielding solutions, the 2014 *RadiCure* randomised trial by Christopoulos et al demonstrated another novel approach to radiation protection. The primary endpoint was operator exposure and they used an audible dosimeter that beeped at certain dose thresholds. It was worn on the front pocket of the lead apron. The 505 patients were randomised for whether the operator wore the dosimeter or not. First and second operator exposure was significantly lower (36% and 29% respectively) when the dosimeter was worn. The paper suggests that when the dosimeter beeped, it would trigger the operator to change their position, optimise the shielding, adjust the C-arm position or adjust the X-ray settings. This appears to be a low cost solution that does not impact on everyday practice but does reduce dose.(77)

The use of lead goggles or eye glasses during angiography is recommended by the ICRP as the lens of the eye is relatively radiosensitive.(7) Vano et al found that 38% of Cardiologists had posterior lens opacification in their 2010 study of 58 interventional cardiologists and concluded that there was an urgency in educating interventional staff in radiation protection.(78) An early study in 1984 by Dash et al demonstrated a 35% reduction in radiation dose to the operators eyes with lead glasses during cardiac catheterisation.(79) Additionally, a study by Waddell et al in 2016 demonstrated a 90% reduction in eye dose measured during a phantom study with different styles of lead eye glasses during spine fluoroscopy.(80)

Given that radiation to the operator's brain has received significant attention,(63) lead equivalent protection caps have lately become available. A randomised controlled study investigated the effectiveness of these protection devices, published in a paper by Uthoff et al in 2015. Dosimeters situated inside and outside of the lead caps, which varied in

thickness demonstrated a 91.5% reduction in dose for the 0.3mm lead equivalence and 97.1% for the 0.5mm lead equivalence.(81) This demonstrates the impact of additional shielding devices that can cover areas of the body that traditionally are not protected.

Equipment settings

In the same way that we have seen equipment settings reduce dose to the patient in CA and EP procedures, these settings will also reduce dose to the operator. Abdelaal et al performed a randomised controlled trial in 2014, and randomised 385 patients to have their radial access procedure performed at either 7.5 pps or the more traditional 15 pps for fluoroscopy and cine acquisition was kept at 15 fps in both groups. The results showed that for CA, average operator dose was 21 μSv for the 7.5 pps group and 35 μSv for the 15 pps group. During PCI, these values were 45 and 63 μSv respectively. This demonstrates the impact that lower dose settings can have on operator dose, which would have a significant impact over many years of work.(29)

Overall, the literature surrounding patient radiation dose and occupational exposure to staff performing cardiac angiography and intervention appears to concentrate on the primary operator. Also, they tend to investigate the radiation dose impact of only one particular variable, of which arterial access appears to be the most numerous. No study to date has investigated the multitude of different factors that would impact on radiation dose to the patient and the operator as a holistic all-encompassing approach. This is needed to understand radiation dose and which factors drive the higher doses in the cath lab. High doses to the patient and the operator need to be highlighted and the factors that led to the high dose should be investigated.

In addition, the literature focuses only on the radiation dose to the primary operator. This stands to reason as the operator is the staff member that stands the closest to the X-ray source and the patient. Primary operators, usually the cardiologist performing the procedure, have tableside and ceiling suspended lead shields in place to protect them from the harmful effects of radiation. These are usually only in place on the right side of the procedure table, where the primary operator and their assistant stand. However, there are other members of staff who are also in the cath lab who are also exposed. Some also stand close to the patient, particularly during more complex procedures where anaesthesia is required. During percutaneous interventional procedures for structural pathology of the heart (including left atrial appendage (LAA) occlusion and MitraClip™ implants) require guidance with trans-oesophageal echocardiography (TOE) in addition to fluoroscopy (4,82). The echocardiographer or cardiologist who performs the TOE stand relatively close

to the patient and the X-ray c-arm, as it is necessary for this form of imaging. This exposes the echocardiographer and/or echocardiologist who operate the TOE probe and console to the harmful effects of scattered ionising radiation. Whilst the literature has highlighted the risks of radiation to the staff performing fluoroscopically guided cardiac procedures (63,64,78), none of these studies were inclusive of radiation dose to other staff in attendance, and particularly the TOE operators in this environment. There is often no specific additional protection installed at the head end or left side of the procedure table where the TOE operator would stand. Recent guidelines issued in 2014 by the American Society of Echocardiography have highlighted the risks of radiation to TOE operators and the lack of evidence surrounding radiation dose to TOE operators (83). As with all staff working in the cath lab, they are monitored with optically stimulated luminescent dosimeters (OSL) that are interrogated on a monthly basis. While all staff wear these dosimeters, they do not demonstrate how much radiation dose each staff member may receive on a case by case basis.

Knowing the close proximity of the TOE operator to the scattered radiation source, the authors thought it prudent to measure and monitor radiation doses to TOE operators and the other staff in attendance during these complex and lengthy procedures that use moderately high levels of fluoroscopy and radiation. Boland et al had demonstrated that radiation DAP levels for structural interventional procedures, including TAVI, were consistent with those for PCI procedures.(84) This was an important body of work as it had not been previously performed.

Radiation doses to personnel in attendance for surgical access TAVI procedures was performed in a small study by Drews et al in 2014. In that study, the anaesthetist performed the TOE. As such, the dose to a dedicated TOE operator has not been performed to date in a larger study.(85) Doses to other members of staff that are in attendance for these kind of procedures should be investigated in this rapidly changing environment.

1.4 Radiation dose reduction in electrophysiology procedures

Electrophysiology (EP) procedures, where electrical conductivity of the heart is measured and treated, are traditionally seen as high dose procedures, due to the relatively long fluoroscopy times. A study by Tsapaki et al demonstrated that with high fluoroscopy times, the total dose (KAP/DAP) was highest for radiofrequency ablations (RFA) and higher than for PCI procedures.(86) Smith et al investigated this in more detail, breaking down the RFA procedures into groups and compared against diagnostic coronary angiography, which was higher than most RFA procedures, with the exception of ablation for atrial fibrillation, which was higher. A large meta-analysis was performed by Pantos et al in 2009 who investigated radiation doses from 72 cardiac publications. The findings in that study differ somewhat to those above. It found 17 studies related to RFA procedures and quoted an average DAP value of 54.6 $Gycm^2$ and a fluoroscopy time of 45.8 minutes, compared to 4.7 minutes and a DAP of 39.9 $Gycm^2$ for CA. Average fluoroscopy time for PCI procedures in this analysis was 15 minutes, yet the DAP was 78.3 $Gycm^2$. One of the main findings of this analysis was that there is a large variation in radiation dose values between studies. This leads to the comparative differences in the literature when comparing CA and PCI doses to RFA.

Radiation dose reduction for patients undergoing cardiac angiography, intervention and electrophysiology can be achieved in many ways. Firstly, establishing whether the patient needs the examination performed is essential,(7) and informing the patient of the risks and obtaining their consent is also important.(2,7) In a more practical way, during procedures, minimising beam on time, using correct X-ray equipment settings and beam geometry is crucial. In addition, using modern X-ray equipment, that is well maintained and has good radiation dose reduction features are also important.(2)

Some simple changes can significantly reduce radiation dose during electrophysiology procedures. For example; Walters et al demonstrated in 2012 that by simply collimating the X-ray beam during procedures, with seemingly no other changes can reduce the radiation dose rate by 37% for simple ablation procedures.(87)

Removing the stationary grid

There are other ways in which radiation dose can be reduced, such as removing the stationary grid, which has been demonstrated previously several times.(39,88,89) The first, as previously mentioned in **chapter 1.2,** was by Partridge et al in 2006, who compared radiation doses and image quality during coronary angiography and intervention with the

grid in and with the grid out. For the grid out procedures and air gap was used to minimise image noise. Similar image quality was obtained for approximately a 50% dose reduction during CA.(39) The second study by Rogers et al removed the stationary grid and a low frame rate protocol was used as a combined approach to reduce dose for electrophysiology procedures. This study also demonstrated significant decrease in radiation dose with this method of dose reduction; up to 65% with phantom measurements and a similar reduction under clinical practice.(88)

X-ray equipment optimisation

Optimising X-ray equipment settings can have dramatic effects of radiation dose. Primarily, this is driven by how much radiation the X-ray machine uses to create an image and the number of pulses of radiation that is made per second. The equipment can either be configured by the manufacturer and in some cases the end user can adjust these factors to optimise the image.

The routine use of collimation is also advocated in review and consensus publications.(2,7,69) Walters et al demonstrated practically what results can be obtained through effective collimation during electrophysiology procedures. Their study compared the reduction through collimation strategies made by one operator in comparison to three other operators that did not routinely use beam collimation. The study demonstrated a 37% reduction for simple RFA and 12% for complex ablation procedures and advocated its routine use.(87)

Cardiovascular X-ray systems with image intensifiers adjust the image quality using an automatic brightness control system within the image intensifier.(2) On the other hand, some more modern cardio-vascular X-ray systems can be configured to alter many different factors of the x-ray beam. The number of x-ray pulses per second, the number and the penetration power of the x-ray photons and even the contrast and edge enhancement of the resultant image can all be adjusted mid procedure. Together, these beam properties will affect the overall radiation dose as well as the resulting image quality. In order to achieve low dose procedures in electrophysiology, an X-ray system’s fluoroscopy pulse rate can be substantially lower and the dose per pulse can be lower than for coronary imaging. A fluoroscopy dose rate of 2 or 3 pulses per second is advocated by Heidbuchel et al in their 2014 practical guide in the European Heart journal. (69)

Reducing the pulse/frame rate has been reported in multiple publications, though these were usually part of a multitude of changes to practice to produce a dose reduction.

Schneider et al reduced their frame rate from 7.5 pulses per second (pps) to 4 pps in addition to shorter cine times and greater use of the 3 dimensional mapping system. A 90% dose reduction was obtained with these strategies implemented, though it is not certain what proportion is attributed to the lower pulse rate.(90) Rogers et al reduced their frame rate from 12.5 pps to 6.25 pps and in addition removed the stationary grid, achieving a 65% dose reduction.(88) Using a similar methodology, in 2017, Attanasio et al reduced the pulse rate from 4 to 2 pulses per second, lowered the detector dose and removed the stationary grid. This resulted in a 73% for cardiac rhythm device implants.(91) The study by Nof et al, in a cohort of 212 patients used a lower dose per pulse protocol to demonstrate that doses for EP procedures could be lowered by 62% and that other factors such as LAO projections and high BMI patients significantly impacted on dose.(92) However, one study by Bourier et al in 2015 only changed the X-ray settings, by lowering detector input dose used by the X-ray system from 23nGy per pulse to 8nGy per pulse for fluoroscopy. They also reduced the cine dose from 120nGy per frame to 36nGy per frame. In addition, they used fluoroscopy pulse rates of just 3 pps and cine frame rates of 7.5 fps. The result was that for ablation procedures, overall radiation dose was reduced by 77%. However, the study did not include other procedures, such as pacemakers and CRT device implants but it does demonstrate that radiation dose per frame can be reduced to much lower levels that previously used.(93)

Three-dimensional mapping

The use of three-dimensional mapping in RFA has demonstrated some significant reductions in radiation dose and fluoroscopy time. The NO PARTY randomised controlled trial published in 2016 demonstrated the effectiveness of 3D mapping and the impact on lowering radiation dose during SVT ablation. This was an important study as it used Monte Carlo simulation for calculation of effective doses and lifetime attributable risk of cancer, the only study to do so on this topic. It estimated that the lifetime attributable risk of cancer was reduced by 96% with the use of 3D mapping.(94) Early et al demonstrated that 3D mapping can significantly reduce the radiation dose for ablation procedures as early as 2006, with the Nax X (St Jude medical, St Paul, MN, USA) system demonstrating the greatest reduction in radiation dose when compared to no 3D mapping and to the Carto system (Biosense Webster, Diamond Bar, CA, USA). (95) Other studies have demonstrated that ablation can be performed without any fluoroscopy at all, such as the 2010 study by Reddy et al, who demonstrated that ablation of atrial fibrillation can be achieved using just intra cardiac ultrasound and 3D mapping, using the Nav X system.

(96) Using the UNIVU (fluoro integrated three dimensional electroanatomical mapping system) module, as an add on capability to the Carto system and can aid non-fluoroscopic imaging during electrophysiology procedures, as it uses pre-recorded fluoroscopy to superimpose the 3D map onto. Huo et al demonstrated a 73% reduction in radiation dose using the Carto 3 (Biosense Webster, inc, Diamond Bar, CA) system, from 2440cGycm2 to 652 CGycm2 for AF ablation procedures in a randomised controlled trial.(97) The same system, in a separate study by Christoph et al in 2015 demonstrated similar reductions in radiation dose across a multitude of different ablation procedures.(98)

Magnetic guidance systems

Other non-fluoroscopic magnetic guidance systems, such as the *Mediguide*™ system (*Mediguide*™, St Jude Medical, St Paul, MN, USA) have also recently emerged as additional technologies that allows catheters to be displayed in real time. It uses pre-recorded fluoroscopic loop images and electromagnetic signals, without further use of fluoroscopy.(99) The resulting radiation dose reductions resulting from using the *Mediguide*™ system are impressive. In 2013 Vallakati et al reported that their dose reduced by 62% using *Mediguide*™ for supraventricular tachycardia ablations.(100) Sommer et al, also in 2013, saw a greater reduction in fluoroscopy dose, from 996 to 187 $CGycm^2$ during the same types of ablation procedures for supraventricular tachycardia.(101) In 2014 Sommer et al again reported similar radiation dose reductions using *Mediguide*™ for atrial fibrillation ablation procedures in 375 patients.(102)

For Biventricular cardiac resynchronisation therapy (CRT) devices, Butter et al established radiation doses for these procedures. They demonstrated results of 20.3min and 11100 CGycm2 for conventional fluoroscopy guided implants in their study of radiation dose associated with these devices.(103) However, Doring et al implemented the *Mediguide*™ technology to reduce radiation dose during CRT device implantation in a small series of 71 patients. Of those 71, 34 patients were matched against 34 patients that underwent conventional CRT device implantation using traditional fluoroscopy. It demonstrated a significant reduction in radiation dose (338 vs 603 $CGycm^2$) using the *Mediguide*™ system, both of which are far lower than that of Butter et al.(104) Again using the *Mediguide*™ system, in conjunction with a low dose protocol, Thibault et al demonstrated a more impressive 95.9% reduction during CRT device implants.(105) These systems have added significantly to radiation dose reduction in these relatively high dose procedures but they do, however, change working practices and add additional cost to EP laboratory

installations, in addition to the ongoing consumable costs by way of catheter purchase, which must also be considered.

New X-ray system technology

Using new X-ray technology has seen radiation doses reduced significantly, for a range of electrophysiology procedures, without significantly changing working practices.(106,107) Dekker et al demonstrated that doses can be reduced by up to 43%, whilst maintaining image quality, simply through using image processing technology, introduced by one X-ray equipment manufacturer.(107) The same technology was also reported on in 2017 by Sharma et al, who also found significant radiation dose reductions(108) and by Van Dijk in 2016 who saw a 69% reduction in radiation dose with this same type of system. (109) Other than these three publications, measuring the radiation dose reduction after implementing newer X-ray systems is distinctly lacking in the literature. In addition, the radiation doses reported in these studies are not particularly low.

Given the high fluoroscopy times and high doses reported for electrophysiology procedures, they seem an obvious group of procedures to investigate the effectiveness of using more modern X-ray equipment, with low radiation dose settings.

As we can see, reducing radiation dose in EP is complex and multi-factorial. An example of a study that has tied all the dose reduction elements together is that by Thibault et al, published in 2017.(110) They investigated the reduction in radiation dose to patients and staff in their three EP laboratories over a four year period. Changes were implemented in training and awareness, reducing fluoroscopy pulse rates, dose per pulse and investing in 3D mapping and magnetic guidance systems. This was in addition to new X-ray equipment. An 85% reduction in overall DAP was seen across all procedures and in addition, the operator radiation dose was also significantly reduced over that period.(110) This demonstrates what is achievable with a consistent focus on multiple radiation dose reduction strategies.

1.5 Contrast media and acute kidney injury in TAVI procedures.

Iodinated contrast media (ICM) is critical to performing angiography. Injecting this liquid enables physicians to visualise veins, arteries and structures throughout the body. It is generally inert and is excreted by the kidneys. It is, however, toxic to the kidneys.(14) McCulough described contrast media and its effect on renal function in a paper published in 2008.(14) Chronic kidney disease (CKD) is usually a requirement for the development of acute kidney injury (AKI), which is usually identified as a serum creatinine of >1.0 mg/ml in women and >1.3 mg/dl in men. There is a release of adenosine, endothelin and other vasoconstrictors triggered by ICM, which reduces blood flow and the stasis of ICM in the kidney tubules can cause renal tubular cell injury and death. Medullary hypoxia and ischemic injury also results. If this is added to by hypotension, showering of artheroembolic material, or bleeding, this can amplify the process.(14) This is particularly relevant during TAVI procedures, as moderate volumes of ICM are required for device implants. In addition, there are periods of hypotension, caused by rapid burst pacing and there may be showering of artheroembolic material during the procedure. ICM is needed to accurately align the valve plane and position the TAVI device. In addition, the femoral arteries need to be imaged with ICM for device access and to ensure that there is no vascular injury after the large sheath is removed. Patients are often elderly and present with multiple co-morbidities, including renal impairment and CKD.

When reviewing the literature for AKI in TAVI procedures, the majority of studies use the RIFLE criteria to define AKI, which is outlined by the publication by Bellomo et al in 2004.(111) This criterion was created by the Acute Dialysis Quality Initiative group (ADQI). It created a five-tier classification system, starting with *Risk*, followed by *Injury*, then *Failure*, then *Loss* and finally *End stage* renal failure. Serum creatinine levels and urine output are used as quantifiable measures to classify the level of AKI against the RIFLE criterion.(111)

In assessing AKI induced by the TAVI procedure, Aregger used the RIFLE classification,(112) and Bagur et al also used the RIFLE criteria in their 2010 study. (>25% reduction in estimated glomerular filtration rate (eGFR) at 48 hours post procedure). The valve academic research consortium (VARC-2) outline classifications and inclusions for all TAVI related outcomes and complications. Their criteria outlined in the 2013 publication by Kappetain et al include a definition of the stages of AKI, which is also based on the RIFLE classification. The AKI definitions outlined by the VARC-2 are stated as an increase in

serum creatinine of 150-200% (stage 1), 200-300% (stage 2) or >300% (stage 3).(113) Other studies have used different scoring systems to define AKI in relation to contrast induced nephropathy (CIN). For example, Madershahian et al used the European Society of Urogenital Radiology guidelines in their 2014 study of CIN during TAVI, which used an increase in serum creatinine of 25% or greater over three days after exposure to Iodinated contrast media, which is the same as the RIFLE classification.(114) It is therefore important to use a common classification system or at least have an awareness of any differences in classification systems when comparing outcomes of AKI in the literature.

Because of the relationship between ICM and AKI, accurate documentation of the total volume of contrast media used for the TAVI procedure is very important. Total contrast media volumes used for TAVI procedures vary greatly in the literature and the impact that contrast media has on acute kidney injury for TAVI is not entirely conclusive. One of the first studies that reported on acute kidney injury (AKI) was that by Aregger et al in 2009 on 58 TAVI patients. They reported a 28% incidence of AKI, which under multivariate logistic regression was associated with a surgical approach, thrombopaenia and pathalogical leucocyte count. Interestingly, iodinated contrast media volume (ICM) was not significantly higher in patients that suffered AKI.(112) This finding was similar to that in the study by Bagur et al in 2010. In their study of 213 patients, average contrast media volume was 97 cc and AKI incidence was 11.7%. Again, ICM volume was not significantly different between those that had AKI and those that did not. AKI was an independent risk factor for mortality and was associated with hypertension, chronic obstructive pulmonary disease (COPD) and the requirement for blood transfusions.(115) Kong et al demonstrated a higher median volume of 219 cc in their cohort of 52 patients undergoing TAVI in 2012. In their population, 15 patients had acute kidney injury (AKI) and AKI was associated with procedural technique and blood transfusion. The contrast media volume in the AKI group was higher (279 cc vs 216 cc), though it did not reach significance (p=0.50).(116) Vontobel et al went a step further in assessing contrast media induced AKI in their 2015 publication. In that study, contrast media volumes associated with the pre-operative computed tomography (CT) scan and angiography, in addition to the contrast media volume used for the TAVI procedure were assessed. In 257 patients, AKI occurred in 31 patients. Median ICM volume including that within 5 days prior to TAVI, and the TAVI procedure was relatively low at 144cc and again there was no significant difference in contrast media volume between those that had AKI and those that did not (154ml vs 139.5 ml, p=0.77). (117) Finally, a meta-analysis by Thongprayoon et al in 2016 which specifically analysed

four studies that investigated the impact of contrast media volume on AKI found that ICM volume was not likely to play a role in TAVI related AKI.(118)

The use of iso-osmolar contrast media (IOCM) has previously been associated with lower rates of contrast induced nephropathy in patients with poor renal function by in a meta-analysis by McCullough et al in 2006.(119) However, Reed et al performed a meta-analysis, including 2763 subjects from 16 randomised controlled trials, suggesting that ICOM is not associated with contrast induced kidney injury.(120) Heinrich et al also performed a meta- analysis in 2009 and also concluded that of 25 trials identified, IOCM was not associated with lower rates of contrast induced nephropathy (CIN).(121) In TAVI, only one study has compared IOCM with low osmolar contrast media (LOCM). That study, by Chatani et al in 2015, compared 203 patients, half with ICOM and half with LOCM. Though not randomised, there was equal amounts of contrast media administered (269cc vs 288cc p=0.12) and there was no significant difference in the rates of AKI between the groups. Only the pre-procedure creatinine level was predictive of AKI in that study.(122)

In an effort to reduce the incidence of AKI, forced diuresis has been assessed in patients undergoing TAVI using the Renal-guard system. A publication by Barbanti et al in 2015 outlined the concept of the Renal-guard system, which is one of inducing diuresis with Frusemide (0.25mg/kg) to achieve a urine flow rate of 300ml/hour. This is matched with isotonic intravenous hydration.(123) This system was compared in a randomised trial (RPOTECT-TAVI) to standard hydration. The Renal-guard group had an AKI rate of 5.4% vs 25% in the control group, demonstrating its effectiveness.(123) Visconti et al also investigated the Renal-guard system in 2015, in 22 patients versus 26 patients that were the control group. The Renal-guard group were those with renal impairment and they found that AKI was present in 38.5% of patients in the control group vs 4.5% in the Renal-guard group. This is particularly interesting because the Renal-guard system was used only in patients with renal impairment, whereas the control group did not have renal impairment.(124) Chorin et al also investigated the Renal-guard system in their 2017 publication. Their study investigated the Renal-guard system during 150 CA, PCI and TAVI procedures against a patient matched population that did not use the Renal-guard system. They found that the Renal-guard system reduced AKI in all procedure groups. Interestingly, they also found that the volume of ICM did not correlate to AKI incidence.(125) A meta-analysis of the Renal-guard system was performed in 2017 by Putzu et al and included 4 randomised studies investigating the effectiveness of the

system. The overall finding was that the Renal-guard system reduced contrast-induced AKI in patients with renal impairment prior to coronary procedures and all patients undergoing TAVI. It noted, however, that further randomised controlled trials should be performed.(126)

Patient gender may also play a part in AKI. In 2014 Madershahian et al investigated the relative risk of CIN in females to males with pre-existing renal impairment during trans-apical access TAVI. Their study found that women received more contrast media than men when compared to their body size and that CIN was higher in women than men and was associated with a higher 60 day mortality. Their study cohort, however was relatively small (n=55) which made extensive univariate and multivariate analysis difficult.(114)

Rather than focusing on AKI, Faillace et al investigated whether there may actually be an improvement in renal function following TAVI. Their 2017 study of 69 patients using the VARC 2 criteria found that overall, more patients saw an improvement in renal function than renal dysfunction and that 90% of patients left hospital with similar renal function or an improvement in real function.(127) There is a lack of evidence of contrast media usage and AKI rates in TAVI procedures in Australia and this should be investigated.

Looking to the future: TAVI has been successfully reported without using any contrast media. Eskandari reported in 2016 how they used fluoroscopy and echocardiography using the *Echonavigator* software developed by *Philips Healthcare*. This software overlays the 3 dimensional Trans Oesophageal Echocardiography (TOE) images onto the fluoroscopy image, negating the need for visualisation of the aortic anatomy with ICM. In their report, two procedures were performed using this technique and both had no change in their renal function.(128)

1.6 The use of rotational angiography during TAVI procedures

The iliac and femoral arteries are the access route of choice for trans-catheter aortic valve replacement (TAVI), as this percutaneous option is less invasive than the surgical alternatives.(129) Assessment of the ilio-femoral arteries is therefore of utmost importance, as the size of the original TAVI delivery sheaths were large; 22 to 24 French. In the original PARTNER trial, vascular complications occurred in over 30% of procedures, (3) which highlights the importance of adequate imaging of these arteries prior to TAVI. As described by Delgardo et al in 2010; standard angiography (2D angiography) is a frontline tool in evaluating the femoral arteries but it does not provide information on the soft tissue structures, such as calcification. Multi-slice computed tomography (MSCT) on the other hand has benefits as it can provide information on the vessel size, degree of tortuosity and the vessel calcification.(129) In 2010, a guidance paper was published for assessing patients for aortic valve implantation by Kaleschke et al. They outlined the use of 2D angiography to assess femoral artery calibre and tortuosity and that biplane angiography would be superior to single plane angiography, as it may be better in assessing the vessel course and eccentricity.(130) With regard to multi-slice computed tomography (MSCT), their article suggests that MSCT should be performed if 2D angiography suggests suitability or if angiography is not available. It states that MSCT allows for precise measurements and an evaluation of the course of the artery and that 3-dimensional (3D) reconstruction may be useful. Their summary goes on to describe the usefulness of each of the imaging modalities.(130)

Delgardo et al described echocardiography as the cornerstone of valvular imaging for TAVI and that at the time, there was '*growing interest'* in MSCT. It did however comment that MSCT can evaluate the descending aorta and femoral arteries and that MSCT and MRI are the gold standard, as they give multi-planar imaging.(129) MSCT is described as the most comprehensive modality at assessing all aspects of TAVI imaging, though it does have issues with contrast loading in patients with renal impairment.(129) 2D angiography is however particularly useful in assessing the arteries post TAVI, as it can assess any residual bleeding post TAVI, as described by Lareyre et al in 2017.(131)

Moving forwards to 2012 and Achenbach et al describe in an expert consensus statement, that the main indication for MSCT in TAVI is for evaluation of the access route, whether surgical or percutaneous in addition to assessment of the native valve anatomy.(132) In 2013, Leipsic et al summarised the role of CT for predicting complications in TAVI. Again,

this publication highlighted the deficiencies of 2D angiography in imaging calcification and tortuosity. This publication highlighted the importance of MSCT in evaluating the ilio-femoral arteries and that these arteries should be measured in the true cross section of the artery and not just in the transverse axial plane. Also, it describes the ability of MSCT to be able to adjust the 'windowing' of the acquired image to reduce partial volume averaging of calcified areas of the artery and that identification of horseshoe circumferential calcification as is a major predictor of vascular complications.(133)

As discussed in the previous section, patients undergoing TAVI procedures are elderly with multiple co-morbidities, including renal impairment. Reducing the volume of ICM is as important during the patient work-up phase as it is during the TAVI procedure. Nietlispach et al demonstrated in 2009 that a direct injection to iliac artery using a pigtail catheter can significantly reduce the contrast volume required for imaging the ilio-femoral tree with MSCT. This was achieved by inserting a pigtail catheter during the angiogram examination and then transferring the patient to a CT scanner. Only 15-20 ml was required for the additional MSCT images, yielding additional information on the vessel lumen size and calcification.(134)

At this time, the authors hypothesised using rotational angiography (cone-beam CT) to evaluate the ilio-femoral arteries. Rotational angiography can readily be performed as part of the femoral angiography examination, if the X-ray system supports it. Because the injection of iodinated contrast media (ICM) is direct, much lower volumes may be permitted. Rotational angiography, DynaCT, C-arm CT and cone-beam CT are different naming conventions for essentially the same imaging modality. It is the description of using the angiographic flat detector, found in many interventional suites, to create volumetric data sets by rotating it around the patient. Isotropic (multiplanar) reconstructions and 3D images can then be created.(135) Binder et al's 2012 paper used rotational angiography (DynaCT) to evaluate the aortic root anatomy and determine an appropriate implant angle for TAVI. This was compared to MSCT and both modalities were then compared to the actual post implant projection. There was a significant correlation between the DynaCT projection and the MSCT projections. There was also a slight but significant difference between the modalities in terms of predicted implant angle, though this was deemed not to be clinically relevant.(136)

Using rotational angiography to achieve a suitable implant projection was assessed in 2012 by Poon et al.(137) That study used rotational angiography in the assessment of the aortic root to obtain a perpendicular imaging plane for implant of the TAVI device. In that

study, patients underwent rotational angiography (DynaCT) as part of the TAVI procedure and a 3D image was created. Specialised '*aortic valve guide'* software was used to determine an appropriate C-arm angle for the TAVI implant. The implant angle was also determined using MSCT and any differences were recorded. Using the post implant image as a guide, the appropriateness of the implant angle was assessed. The study found that peri-operative DynaCT was superior to MSCT at predicting an implant angle and it also found that those patients whose implant angle was not scored as excellent had a greater degree of paravalvular regurgitation. The study determined that DynaCT with the aortic valve guide software was more likely to achieve an excellent implant angle, thus demonstrating that the use of DynaCT could actually improve clinical outcomes.(137)

DynaCT has been used in the assessment of arteries in other specialties. Nordon et al performed a study in 2010 examining the feasibility of using intra-operative DynaCT for the assessment of abdominal aortic aneurysm (AAA) repair. Their study on 20 consecutive patients assessed 17 specific morphological variables. They found that DynaCT was adequate in assessing the aorta prior to endo-vascular aortic repair (EVAR) and that it's use may be particularly useful in the emergent setting. They did find, however that the detector size may be too small and that the image quality/resolution was not as good as MSCT. They found that its greatest limitation was in the assessment of the ilio-femoral arteries and the underestimation of calcification.(138)

Wiegerinck et al published a study in 2014 which compared MSCT and angiography for the assessment of the ilio-femoral arteries. In 102 patients, 700 measures were taken with both MSCT and angiography. They used 3mensio software for the MSCT measurements and found that on average, MSCT measures were 1.7 mm smaller than angiography and that subsequently, 18 patients arteries were smaller than 6mm in diameter on MSCT. This excluded them from TAVI implant but these patients measured greater than 6mm on angiography. 15 of these patients went on to have a successful TAVI procedure via the femoral artery.(139)

Okuyama et al demonstrated in 2014 that MSCT with contrast media was better able to predict vascular complications than patients who underwent non-contrast MSCT and 2D angiography. Their study also found that contrast MSCT and non-contrast MSCT both measured vessels slightly larger than on 2D angiography,(140) which is different to the findings of Wiegerinck et al (139). It appears that the differences in measurements obtained between modalities is still not definitive.

Further applications of DynaCT have been reported with regard to TAVI. In 2015, Abu Saleh et al described a technique of using co-registration technology to fuse the MSCT and non-contrast DynaCT images together. This was used in surgical access TAVI procedures. It allows the outline of the aorta and the ideal puncture site to be overlaid onto the fluoroscopy image. This aided the direct puncture of the aorta and was found to be accurate and its use led to a lower volume of contrast media being used in those cases.(141)

DynaCT has also seen a role in the treatment of paravalvular regurgitation, using the co-registration of MSCT and DynaCT images. Van Leer-Greenberg et al describe a case study in 2014 where the MSCT was used to identify the paravalvular leak location and by using DynaCT and co-registration the outline of the aorta and a marker identified the leak site. The C-arm was then positioned to ideally visualise the passing of a catheter across the leak site. The leak was then successfully closed without further complication. This is a good example of the integration of the different modalities and was particularly useful in this case, as there were no radio-opaque anatomic markers on the valve in question. (142)

1.7 X-ray beam distortion in TAVI

X-ray systems use a small focal spot size for a sharp image, which projects a beam of X-ray photons. This beam is then collimated using lead filters to the desired size to project the X-rays photons onto the film plate or digital detector.(143) Objects near the edge of the image are projected onto the detector with photons travelling obliquely when compared to those at the centre of the beam. Consequently, these objects could appear distorted in shape when visualised on the image.(143) This is termed ‘distortion’ (143) or sometimes this is called the ‘parallax’ effect. According to Buckle et al, parallax is one of a number of illusions in radiology and can be helpful in some situations in radiography but also not helpful as it can degrade image quality. One example is the narrowing of disc spacing of vertebrae that are at the periphery on spine radiographs. Due to the divergent nature of the beam from a point source, the vertebrae size and position appear distorted.(144)

The effect of distortion/parallax is apparent on plain film radiographs. Wells et al performed a study in 1991 investigating the effect of parallax in chest radiographs of children. This was performed in the assessment of a short trachea which is evaluated from antero-posterior chest radiographs. Normally the tracheal bronchial carina on the air bronchogram is superimposed on the T4 or T5 thoracic vertebrae, depending on the child’s age. There was concern that the angle of the incident X-ray beam in relation to the patient could cause a mis-diagnosis of short trachea due to the divergent beam causing distotion/parallax. However, their findings using chest x-rays and also post mortem bronchograms demonstrated that beam angulations of up to 10 or 15 degrees would not cause sufficient parallax to significantly shorten the trachea in relation to the thoracic vertebrae. Therefore, the effect of parallax was not enough to cause incorrect interpretation of a short trachea in normal clinical practice.(145)

In 1994, Rutherford et al reported that using the clavicle to position a central venous line was prone to error on antero-posterior mobile radiographs due to the parallax effect. Instead they proposed using the right main bronchus and trachea as a landmark as it is much closer to the superior vena cava than the clavicles. Using this technique they found that in 5 of 100 patients assessed, the tip of the central line had moved using the clavicles as a landmark on subsequent chest X-rays, though they had not moved using the right main bronchus and trachea landmark. They suggest that this change was due to parallax between the two radiographs in those patients.(146)

In 2008 Petilon et al evaluated the effect of parallax on a spine model and an implanted artificial lumbar disc. Their study found that moving the spine from the centre of the image or by angling the c-arm even by a small amount can give the impression of a poor implant position. Their finding suggested not using the spinous process to determine the midline position and instead use the borders of the vertebral body, which apparently was different to that laid out in surgical technique guide.(147)

Matsushita et al proposed using parallax to create a 3 dimensional image for orthopaedic surgery in 1998. In their study, they developed a mobile C-arm which had two X-ray tubes and each X-ray tube fired separately in an alternate manner at 15 pulses per second onto the image intensifier. Using the parallax effect, when visualising the screen with specialised polarised glasses, a 3 dimensional image was created and this enabled the surgeon to insert inter-medullary nails without needing to move the c-arm. This was beneficial as it enhanced the surgeons visualisation of the bone and because the c-arm is not moved, it does not compromise the sterile field.(148)

The effect of X-ray beam distortion on a TAVI device had not previously been described. The superimposed appearance of the TAVI device after implant is particularly important in confirming that the ascending aorta is perpendicular to the incident X-ray beam. Due to the divergent nature of the X-ray beam, the incident beam may be perpendicular at the centre of the image and objects in the centre of the image will not be distorted. However, as objects are moved further out from the centre, their appearance may be more distorted. This is particularly apparent with the TAVI device, as when they are imaged at the periphery of the field of view, their appearance may take on an appearance that would suggest that the central ray is not perpendicular to the aorta. This is important, as Poon et al pointed out in 2012. Their paper demonstrated that not having the beam perpendicular (coaxial) to the aorta was more likely to lead to paravalvular leak/regurgitation.(137) This is clinically important as the PARTNER trial two-year outcomes demonstrate. The paper by Kodali et al demonstrated that even mild paravalvular regurgitation or aortic regurgitation was associated with increased mortality at 2 years post procedure.(149)

Therefore, special attention should be paid when implanting the TAVI device. A coaxial or perpendicular X-ray C-arm angle ensures that the three coronary sinuses are aligned in one plane under fluoroscopy and the depth of valve implantation in relation to the annulus can be accurately assessed.

Conclusions

When considering the literature as a whole, much research has been performed in relation to radiation doses in cardiac angiography and intervention. However, the X-ray systems we use are evolving continuously and the doses associated with them need continuous audit, particularly in countries like Australia where no national benchmark exists. As new procedures that use X-ray imaging, like TAVI emerge, there are many things that need to be considered, such as the radiation dose to the whole team, in addition to the radiation dose and contrast media dose to the patient. Also, the pre-operative imaging assessment TAVI with traditional tools like MSCT and echocardiography are now well researched and understood but there are still opportunities to explore the imaging capabilities of the angiographic C-arm with these new procedures, both pre-operatively and peri-operatively.

The contents of this thesis are quite unique, as it investigates the aspects of cardiac angiography that are relevant to cardiac radiographers; a niche that fits between the realms of medical physicists and interventional cardiologists.

Chapter 2 –

J. Crowhurst, M. Whitby, D. Thiele, T. Halligan, A. Westerink, S. Crown, J. Milne. Radiation Dose In Coronary Angiography and Intervention: Initial Results From the Establishment of a Multi Centre Diagnostic Reference Level In Queensland Public Hospitals. *J. Med. Radiat. Sci.*, 2014; 61, (3), 135–141

Details of my contribution to authorship.

This chapter encompasses the output of a project sponsored by Allied Health Professions office of Queensland. I wrote the project proposal prior to enrolment to this candidature. Upon approval of the project funding, I took on the role as project officer. I initiated meetings with custodians of the relevant data and local experts on the topic (publication co-authors) to establish study design. I wrote the research protocol and sought and obtained ethical committee approval. I met with relevant stakeholders, met and obtained permission for use of data from these stakeholders.

I performed a literature review of all relevant, previously published material and reviewed current guidelines on reporting such studies. I analysed the data obtained, continued consultation with local experts in the field (co-authors) and wrote up the findings before sending out for critical review by the co-authors. I liaised with the relevant journal for publication as corresponding author and made suggested changes in line with peer review.

Prologue

Before investigating radiation dose and factors that may increase radiation dose or be predictors of high dose, it is important to establish acceptable radiation dose levels that X-ray units use to perform the procedures. This is an important step in radiation dose management and is recommended by the International Committee for Radiation Protection (ICRP)(7). Radiation dose benchmarks that are established locally can be compared to other established benchmark that have been published. Benchmarked levels or diagnostic reference levels (DRLs) are important and they are used a guide as to what radiation dose should be achievable for a particular imaging procedure using X-rays.(7) This was the rationale for the first study of this thesis. No Australian benchmark exists for coronary angiography and intervention and as such the first chapter aimed to establish this.

Radiation Dose In Coronary Angiography and Intervention: Initial Results From the Establishment of a Multi Centre Diagnostic Reference Level In Queensland Public Hospitals

Introduction

Cardiovascular disease (CVD) is the leading cause of death in Australia with coronary artery Disease (CAD), the most common form of CVD being the largest single cause of death(150,151). Invasive coronary angiography (ICA) has been utilised in the diagnosis and treatment of CAD for over 30 years and there is consistent growth in the numbers of these procedures being performed each year(152).

One disadvantage of ICA is the radiation dose to the patient from the fluoroscopy used during the procedure. At high X-ray exposures there is a risk of deterministic radiation effects to the skin, such as erythema, permanent epilation and at very high doses, dermal atrophy and ulceration. There is evidence to suggest that these effects are being increasingly reported (9,21). There is also the increased stochastic risk by way of cancer. The risk of cancer from medical imaging procedures is largely unknown but is related to the cumulative effective dose received from imaging procedures(153). A comparison of the effective doses for medical imaging procedures, including coronary angiography and intervention is demonstrated in **figure 2-1**.

Radiation doses delivered during ICA procedures have not changed significantly over the years and remains one of the highest of any x-ray examination in the acute care setting(6,154). By way of ensuring patient safety, there are maximum permissible x-ray outputs for Cardiac Cath lab (CCL) systems in fluoroscopy mode in Queensland. However there is no such limit for digital acquisitions, where radiation dose can be up to 15 times that of fluoroscopy for the same beam on time(153). Operator dose from scattered radiation from the patient is also a consideration as procedures become more lengthy and complicated. The long term effects by way of cancer to operators from long term exposure to low energy ionising radiation is being increasingly recognised(61,62,155).

Unsurprisingly, radiation protection and advisory bodies suggest that radiation dose for radiological procedures should be monitored closely at a local, regional and national level(7). In order to keep doses low, whilst also maintaining adequate image quality, physicians and their support staff require established, evidence based data to benchmark against and to date in Queensland and Australia, there is no benchmark. The publication

of a benchmark or diagnostic reference level (DRL) has been performed numerous times by radiation regulatory bodies around the world. It is most commonly used in providing a benchmark for diagnostic radiological imaging but can equally be utilised for interventional procedures.(7) They are a guide to good practice,

but are neither dose limits nor thresholds that define competent performance of

the operator or the equipment(7). The DRL provides physicians with a guide for which the median dose of a particular procedure type should fall below and should be used as a tool for optimising patient dose. The DRL is most commonly derived from the dose area product (DAP or PKA) value for fluoroscopy procedures and is a product of the dose output and the area exposed.(7)

The purpose of this study is to establish Queensland Public Facility (Queensland Health) radiation diagnostic reference levels for cardiac catheter procedures, for the purpose of providing benchmarks for ongoing quality assurance and audit.

Methods

Site participation:

All seven public hospitals in the state of Queensland, Australia with a cardiac catheterisation laboratory (CCL) were invited to participate in the study.

Procedures Included:

The study included patients undergoing ICA procedures from January 2013 through to April 2013 inclusive. Procedures were separated into two groups:

- Diagnostic coronary angiography only group (CA)
- Adult patients undergoing Coronary Angiography +/- Left Heart Catheterisation and/or Left Ventriculography.
- Diagnostic coronary angiography in conjunction with single vessel percutaneous coronary intervention (PCI).
- Adult patients undergoing Coronary Angiography +/- Left Heart Catheterisation and/or Left Ventriculography + Percutaneous Coronary Intervention.
- The study included all adult patients that fitted the above criteria. All other procedures, including graft studies and complex multi-vessel PCI were eliminated from the study.

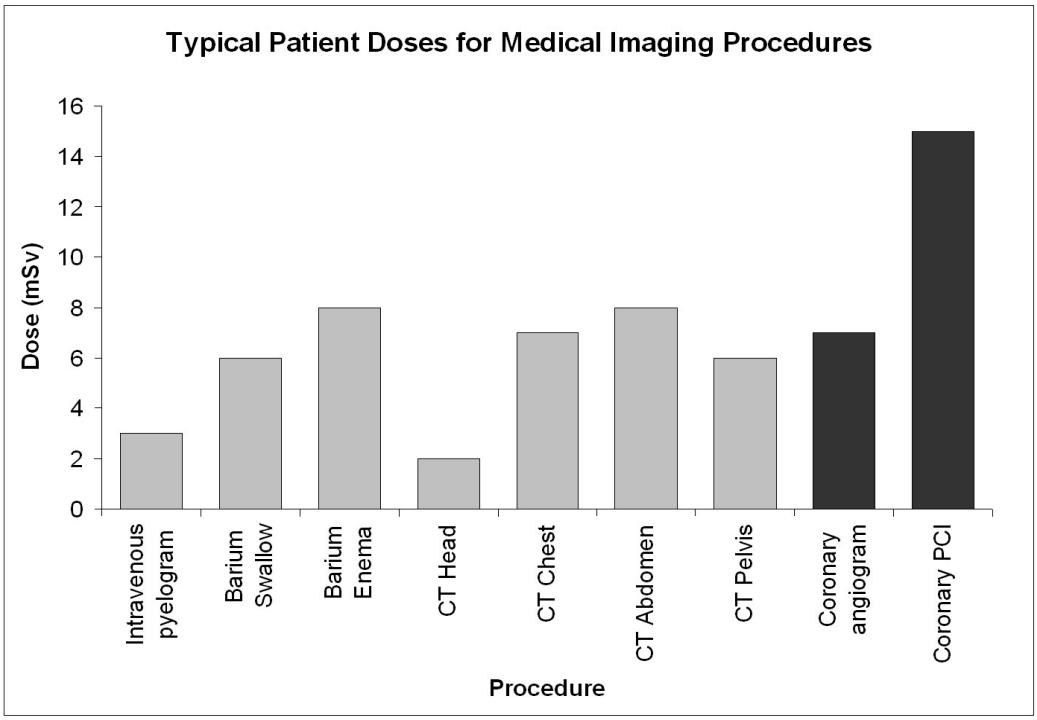


Figure 2. 1 Relative patient effective dose for medical imaging procedures

Legend: Relative patient effective dose for medical imaging procedures. Typical doses for medical imaging procedures. Adapted from data from Mettler et al (6). (mSv = Millisievert, CT = Computed Tomography).

Data Collection:

Radiation data, automatically stored by each X-Ray machine was prospectively entered into an electronic image and reporting system (Impax CV, Agfa Healthcare) at the time of procedure for all cases. Data were extracted from the cardiac catheter laboratory image and reporting system (Oracle database) using structured query language (SQL) and exported into SPSS version 20 for analysis. Radiation data collected were as follows:

- Examination type
- Patient Height/weight/BMI
- Fluoroscopy time
- Dose Area Product (DAP or PKA)
- System calculated skin surface entrance dose (KAR)

Data Analysis

In line with the ICRP recommendations, the DRL was set from the entire population for each procedure and is determined by the 75th percentile of the PKA(7).

Patient size is known to affect dose(21). Therefore patient height, weight and body mass index (BMI) were additional measures for comparison. Fluoroscopy time was collected as it demonstrates 'beam on' time. KAR was measured because in Queensland, the trigger value for a reportable dose and subsequent patient follow-up is determined by exceeding an entrance surface dose of 5Gy. Individual centres were de-identified and allocated a number for analysis.

Additional Measures:

The Dose Area Product meter (DAP meter) housed within the x-ray tube was calibrated on all systems within the 12 months prior to the data collection for each CCL. A variation of ± 25% was deemed acceptable and was in line with similar studies(19,22). CCL X-ray equipment in Queensland Health facilities (QH) is serviced by equipment vendors on a regular basis and the x-ray output of the systems is measured annually by QH radiation physicists to ensure compliance and quality assurance. Ethics approval was granted for this study by the Prince Charles Hospital human research ethics committee, Queensland Health.

Results

All seven QH facilities identified as performing ICA participated in the study, a total of 12 individual x-ray suites. Eleven of the twelve X-ray units were supplied by one manufacturer, with only one from a different manufacturer. All were less than 10 years old and incorporated flat detector technology.

3535 procedures fitted the criteria of the two groups and were included in the study. Of those, 2590 were CA and 947 were PCI. Overall data collection rates for the specified fields were 97.95% in the CA group and 98.33% in the PCI group.

The dose results and patient related data for CA and PCI procedures are demonstrated in **table 2.1.** Distribution curves are demonstrated in **figure 2.2** for the overall populations. How the different facilities/sites contributed to the data is outlined in **table 2.2**. The DRL, as determined by the 75th percentile of the PKA value for the study population was 5865 uGym2 for CA, and 12900 uGym2 for single vessel PCI procedures. How these results compare to the literature is demonstrated in **table 2.3** and **table 2.4**.

Table 2. 1 – Baseline results in this study for the two identified groups, demonstrating the various dose measures collected in this study. Numbers in brackets indicate the inter quartile range.

Measure	Coronary Angoigraphy	Percutaneous Coronary Intervention
Number of Patients	2590	947
Median Patient Age	62.71 (54 – 72)	61.73 (53 – 71)
Median Patient Height (centimetres)	170 (177 - 162)	172 (165 - 178)
Median Patient Weight (Kilograms)	83 (71.0 - 96.0)	82 (73 - 94)
Median Patient BMI	28.7 (24.9 - 32.9)	27.8 (24.8 – 31.9)
Median Fluoro Time (Minutes)	3.5 (2.3 – 6.1)	11.2 (7.7 - 17.4)
Median P_{KA} ($uGym^2$)	3908 (2489 - 5865)	8736 (5449 - 12900)
Median K_{AR} (mGy)	581 (374 - 876)	1501 (928 - 2224)
Calculated DRL ($uGym^2$)	5865	12900

Abbreviations: Numbers in parenthesis indicate the interquartile range. BMI = body mass index, K_{AR} = patient skin surface entrance dose, P_{KA} = dose area product, DRL = diagnostic reference level CA = coronary angiography, PCI = percutaneous coronary intervention,

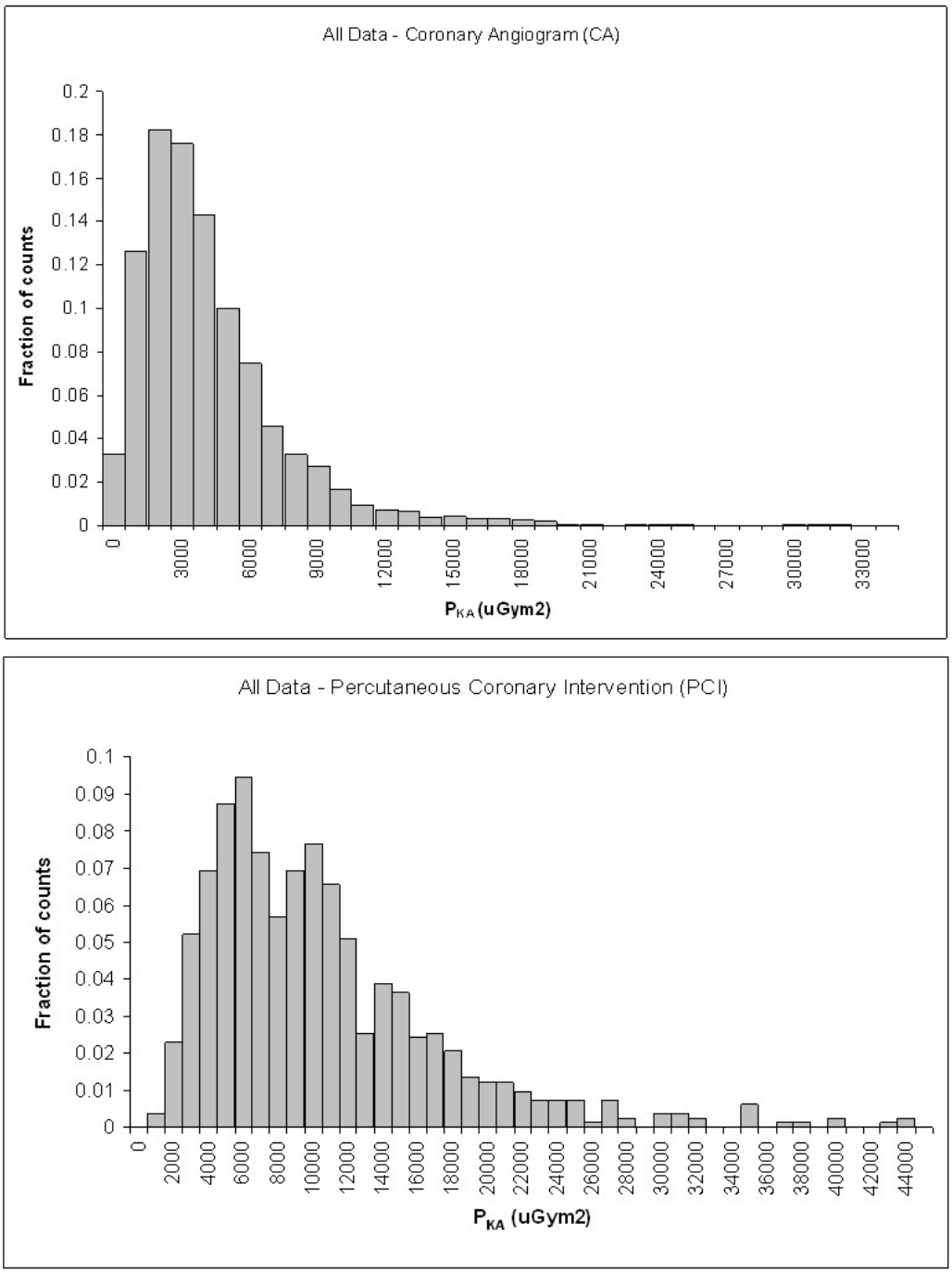


Figure 2. 2 - Distribution plots for CA and PCI procedures

Legend :Distribution charts demonstrating how the distribution of P_{KA} is non normal in both CA and PCI groups. The y axis demonstrates the fraction of procedures that fell within a particular P_{KA} range. (CA = diagnostic coronary angiography, PCI = percutaneous coronary intervention, P_{KA} = dose area product)

Table 2. 2 – How each site enrolled in the study contributed to the data for PKA and the DRL. The values given are all in uGym2.

Diagnostic Coronary Angiography (CA)								
n=	Site 1 (n=193)	Site 2 (n=230)	Site 3 (n=542)	Site 4 (n=331)	Site 5 (n=261)	Site 6 (n=571)	Site 7 (n=462)	All (2590)
Mean	3263	4301	4909	4701	3620	4740	5601	4448
Median	2774	3826	4235	4197	2899	3886	4641	3908
Std. Dev.	2033	2386	3168	2769	2617	3630	4057	2952
25th %	1798	2594	2893	2827	1955	2531	2605	2489
75th %	4178	5472	6288	5788	4461	5779	7176	5865

Percutaneous Coronary Intervention (PCI)								
n=	Site 1 (n=76)	Site 2 (n=127)	Site 3 (n=186)	Site 4 (n=119)	Site 5 (n=68)	Site 6 (n=215)	Site 7 (n=156)	All 947
Mean	8303	10023	10615	10034	6912	12350	8655	9566
Median	7071	8445	9283	8710	6528	10801	7291	8736
Std. Dev.	5111	6177	6986	6401	3483	7580	5690	5918
25th %	4707	5424	5917	5463	4525	6753	4853	5449
75th %	9471	12403	12900	11089	6528	15973	11789	12900

Abbreviations: DRL = diagnostic reference level, P_{KA} = dose area product, Std. Dev. = one standard deviation, 25th% = 25th percentile, 75th% = 75th percentile

Table 2. 3 – Demonstration of how the results from this study compare to those previously published and the country where the data originates. - Diagnostic coronary angiography

CA Group			
Country	Author	Median P_{KA} ($uGym^2$)	75^{th} Percentile
Switzerland (Non-Academic Centres)	Samara et al 2011[14]	5800	10200
USA	Miller et al 2009[15]	4900	8300
Turkey	Bor et al 2008[23]	4910	-
Switzerland (Academic Centres)	Samara et al 2011[14]	4500	9000
Italy	Neofotistou et al 2003[28]	4240	-
Australia	This study	3908	5864
Finland	Neofotistou et al 2003[28]	3960	-
Greece	Neofotistou et al 2003[28]	3800	-
Ireland	Neofotistou et al 2003[28]	3330	-
Ireland	D'Helft et al 2009[5]	3100	4200
Italy	Neofotistou et al 2003[28]	2820	-
Spain	Neofotistou et al 2003[28]	2780	-
United Kingdom	Hart et al 2005[16]	2350	2900
England	Neofotistou et al 2003[28]	1910	-

Abbreviations: CA = coronary angiogram, P_{KA} = Dose Area Product

Table 2. 4 – Demonstration of how the results from this study compare to those previously published and the country where the data originates. - Percutaneous coronary intervention.

PCI Group			
Country	Author	Median P_{KA} ($uGym^2$)	75^{th} Percentile
USA	Miller et al 2009[15]	11700	19300
Turkey	Bor et al 2008[23]	10690	-
Switzerland (Academic Centres)	Samara et al 2011[14]	9000	17000
Australia	This study	8736	12900
Italy	Neofotistou et al 2003[28]	8200	
Switzerland (Non-Academic Centres)	Samara et al 2011[14]	6700	12000
Finland	Neofotistou et al 2003[28]	6690	-
Ireland	Neofotistou et al 2003[28]	4850	-
Italy	Neofotistou et al 2003[28]	4240	-
Ireland	D'Helft et al 2009[5]	4200	8400
United Kingdom	Hart et al 2005[16]	3600	5000
Greece	Neofotistou et al 2003[28]	3900	
Spain	Neofotistou et al 2003[28]	3900	-
England	Neofotistou et al 2003[28]	2710	-

Abbreviations: PCI = percutaneous coronary intervention, P_{KA} = dose area product

Discussion

The investigation and publication of a DRL for coronary angiography has been performed in the UK every 5 years since 1992(18). This has subsequently been followed by studies in Europe(156) and the United States(22). The studies in the UK have found an incremental drop in radiation dose since they started investigating and reporting radiation dose[16].

Many different factors affect radiation dose in ICA procedures and these factors have been evaluated before(157-160). Factors such as x-ray system set-up, operator technique and clinical practice all play a part and it may well be beneficial to locally investigate these factors on a site by site basis in the future**.** Complexity of procedure has also been demonstrated to significantly affect radiation dose(161,162) but again was not measured as part of this initial study.

It is advantageous to collect the height and weight of patients for these studies. Previous studies have normalised their P_{KA} results to patient weight(163). This is in line with a paper by Chapple et al to an average of 70Kg(24). Normalising the dose to a particular patient weight is advantageous for a comparison between x-ray systems. Normalising the dose data to a reference patient weight is difficult with a large number of facilities. Most multi-centre studies have not elected to do this(20,22,25,26) and this was not performed as part of this study. A higher P_{KA} value than some of the literature may be the result, due to the higher median patient weight of 83Kg seen in this study. Another method utilised to normalise the P_{KA} data is to exclude patients outside a weight range of 80Kg ± 5, with the same aim(18). Normalizing may not be logical in establishing a DRL for practical routine use, as the DRL would only relevant to a small portion of patients that fall within a certain weight range.

The results obtained from this study are comparable with those from other studies in the literature. Tables three and four show how this study compares to similar studies. It is evident that there is a great variation between these multi-centre studies. As an example, reference levels for CA range from between 2900 ųGym^2 to 10200 ųGym^2 , with this study sitting just below the average of 6744 ųGym^2 at 5865 ųGym^2. Neofotistou et al attributed higher doses to teaching hospitals in its study,(20) as it is known that in their first year of training operators use higher levels of radiation due to extended fluoroscopy(164). It is noteworthy therefore that all seven facilities involved in this study are teaching hospitals, training registrars and fellows in ICA and this has the potential to make some impact on the results. Neofotistou et al also attributed the possible difference in dose between the highest and lowest centres in its study to the dose rate under fluoroscopy[28]. Although

dose rates of individual x-ray units were not measured in this study, all units are measured annually in terms of fluoroscopy dose, which is governed by state regulations. Sample size may also be important. There are differences in study population size within the literature, with sample sizes for CA examinations ranging from 311 patients(19) to 34236 patients(18). It has been proposed that only 50 examinations will produce sufficient statistical power in these kind of studies(165). With that in mind, the sample sizes of 2590 CA examinations and 947 PCI examinations seen in this study should make one confident that the DRLs calculated here are based on a sufficiently sound sample size.

This study would indicate that Queensland public facilities are delivering appropriate levels of radiation to patients during ICA procedures. However, there is always work that can be done to reduce dose and audits such as this are a good starting point in raising awareness. They are a fundamental foundation for ongoing audits as part of a quality assurance program for radiation dose(7).

In line with recommendations(7), it is planned that doses for cardiac angiography and intervention be measured against benchmarks on an annual basis and for a study such as this to be repeated in 3-5 years. The DRL should be seen a guideline only, as it is well recognised that fluoroscopy procedures are difficult to benchmark and that each individual procedure may deviate from the DRL for many legitimate reasons(7). DRLs are intended to provide guidance on what is achievable with current good practice rather than optimum performance(7). However, to date there is no DRL for these procedures in Australia and this study could be used as an interim yardstick for other cardiac catheter laboratories in Queensland and Australia, until a larger national study can be performed.

Conclusion

This study allowed for the calculation of a DRL for diagnostic and interventional coronary angiography procedures in Queensland Health facilities. The establishment of a benchmark means that these DRLs can be used for ongoing audit in these and new facilities across Queensland and potentially other similar facilities in Australia.

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Limitations

This was a retrospective analysis of a state-wide database and not prospective in nature. The number of procedures from each centre are not equal, which would have been more ideal.

Current implications

More recently, in 2017 the ICRP published guidelines for the calculation of DRLs, which included both diagnostic and interventional fluoroscopically guided procedures. They suggested using the P_{KA} or the K_{ar} as measures to determine the DRL and that dose data can be normalized to patient body habitus but similar results can be obtained without normalization. They suggest that using both P_{KA} and the K_{ar} would be useful in determining why the dose may not be optimized.(27) In addition, other similar studies have emerged: A study has been published by Ngaile et al in 2018, with a DRL for Tanzania, with median values for CA of 37.8 Gycm2 for CA and 86.5 for PCI, which are relatively similar to those seen in this chapter.(17) As at April 2020, there are other DRL or data sets published in Australia with regard to coronary angiography and coronary intervention.

Chapter 3 –

J. Crowhurst, M.Whitby, M.Savage, D.Murdoch, B.Robinson, E. Shaw, N. Gaikwad, R. Saireddy, Hay, K, Walters, D. Factors Contributing to Patient and Operator Dose During Diagnostic Cardiac Angiography. *J Med Radiat Sci.* 2019 66 1： 20-29 doi: 10.1002/jmrs.315

Details of my contribution to authorship:

This chapter was assisted with a research scholarship from the Australian Society of Medical Imaging and Radiation Therapy. For the research scholarship, I wrote a research study outline and protocol after reviewing current literature. I designed the study in consultation with local experts (co-authors). I wrote the research protocol and sought and obtained ethical committee approval.

I performed a literature review of all relevant, previously published material and reviewed current guidelines. I led the collection of the data, analysed the data obtained, performed calculations and statistical analysis, following advice from a statistician. I continued consultation with local experts in the field (co-authors) and as lead author, wrote up the findings before sending out the manuscript for critical review by the co-authors. I liaised with the relevant journal for publication as corresponding author and made suggested changes in line with peer review.

Prologue

Now that local reference levels for coronary angiography and intervention have been established, it is important that efforts are made to investigate what factors during angiography could push doses above the reference level. The study in chapter 2 established the reference level at the 75th percentile of the dose area product.(166) Therefore, the next step in this thesis was to investigate which of the multitude of factors are most likely to lead to a high (above the 75th percentile) radiation dose. In addition, given some recent high profile publications on operator radiation dose,(63,64) it was deemed important to investigate the primary operator's dose and factors that would lead to them having a high (above the 75th percentile) dose. The following body of work investigates this in detail and demonstrates how some factors are predictors of both a high patient and operator dose.

Factors Contributing to Radiation Dose for Patients and Operators During Diagnostic Cardiac Angiography.

Introduction

Cardiovascular disease is Australia's most common chronic disease and coronary artery disease is the leading cause of mortality.(167) Coronary artery disease can be diagnosed and treated in the same setting with invasive cardiac angiography (CA). CA uses X-ray fluoroscopy and carries risks to the patient undergoing these procedures(2). The side effects of radiation are both stochastic (neoplasm and heritable abnormalities) and tissue injury (deterministic).(2) The associated radiation dose and relative risk of malignancy may not be conclusive(168) but the deterministic effects of fluoroscopy procedures, presenting as skin injury have been reported many times(10,12,169) and have been compiled into case review reports and recommendation documents.(2,9) The cardiologist who is closest to the X-ray source and patient is exposed to the harmful effects of low energy scattered radiation during CA which has been highlighted in numerous studies and reports.(63,64,78)

The International Commission on Radiological Protection recommends that dosimeters should be available for all staff working in fluoroscopic laboratories. In addition, a quality assurance (QA) program should ensure the use of dosimeters with a review of abnormal dose values.(7) Dosimeters, using thermo-luminescent or more recently optically stimulated luminescent dosimetry techniques are required to be worn by catheter laboratory personnel. These are submitted for evaluation on a monthly basis. However, these monthly readings do not demonstrate how radiation dose is received on a case by case basis and which factors increase a staff members' radiation exposure more than others.

Patient and operator dose have been investigated before, such as the REVERE trial(170) and the RAD-MATRIX trial,(67) which investigated the impact of vascular access site on radiation dose. However, there is a paucity of data on this subject where all variables that may impact on operator dose are assessed together, and which variables are predictive of high doses.

This study aimed to supplement the QA program and perform a more detailed investigation of radiation exposure to both patients and operators during contemporary diagnostic cardiac angiography procedures. This study sought to identify patient and

procedural factors that may impact on patient and operator dose in addition to identifying which variables are predictive of a high patient and operator radiation dose.

Method:

The study was a retrospective analysis of consecutive patients presenting to the cardiac catheterisation laboratories in this single, tertiary, teaching hospital that had diagnostic procedures performed. Data were collected from mid-August 2014 through to mid December 2015. Approval for this study was granted by the facility human research ethics committee.

Radiation protection for operators

The examination table had lead drapes fitted to the tableside. Operators also had a lead acrylic, ceiling suspended shield. Operators all wore a protective apron of at least 0.5 mm lead equivalent at the front, thyroid shields, lead shin guards, lead eye glasses and some wore lead equivalent protective hats.

Workflow and equipment protocols

All procedures were performed in one of two identical biplane cardiac catheterisation laboratories (Siemens Axiom Artis dBc, Siemens Healthcare, Erlangen, Germany). Operators positioned (panned) the patient on the floating top tables and activated the fluoroscopy and digital acquisition. Radiographers operated the C-arm, controlled pulse rate, dose per pulse, collimation and wedge filtration from an adjacent control room. Fluoroscopy was typically set to 7.5 pulses per second and the digital acquisition (DA) frame rate was set to 15 frames per second. A standard fluoroscopy and acquisition protocol was typically used for procedures in which the X-ray system automatically adjusted copper filtration, kV and mA to achieve a detector dose that would produce an acceptable image.

Radiation data collected were:

Fluoroscopy time (FT), Kerma area product (P_{KA}), skin entrance dose (air kerma - mGy) at the reference point (K_{AR}) and number of DA. These were entered into an oracle database at the end of each procedure (Impax CV, Agfa Healthcare, Netherlands). P_{KA} was the primary measure for patient dose and was calculated using the P_{KA} meter in the X-ray tube

housing and is given in Gycm^2. Both X-ray systems were checked for accuracy of the P_{KA} meter readings as part of their annual compliance tests.

Individual elements for each procedure were entered into the database using a series of tick boxes and procedures were then grouped into 10 categories:

- Abdominal/femoral angiogram only (AFA).
- Coronary angiography only (CORS).
- Coronary angiography + aortogram/ left ventriculogram (CORS-LV/AO).
- Coronary angiography + left heart catheterisation + Right heart catheterisation (CORS-LHC/RHC).
- Coronary angiography + additional coronary artery lesion assessment with intravascular ultrasound (IVUS), optical coherence tomography (OCT) of fractional flow reserve (FFR) - (CORS-OCT/IVUS/FFR).
- Coronary angiography + pulmonary angiography (CORS-PA)
- Coronary angiography + coronary artery bypass graft angiography (CORS-GRAFTS).
- Pulmonary angiography alone (PA).
- Right heart catheterisation +/- venography (RHC)
- Work-up for transcatheter aortic valve implant: Includes coronary angiography, aortography, ilio-femoral angiography (TAVI-WU).

The CORS group was used as the reference group for statistical analysis. Other procedural variables that could impact on radiation dose, such as catheter access route and whether biplane angiography was used were also recorded. Patient variables, including age and body mass index (BMI) were collected. BMI was grouped into three categories: <25, 25-30, and >30 kg/m^2.

Operator dose analysis

The primary and secondary operators (where a second operator was present) were monitored using instantly downloadable personal dosimeters (IDD) (Instadose^{TM}, Mirion technologies, Georgia, USA) in addition to their usual TLD monitors. The IDD was worn on the thyroid collar, on the outside of the protective apron for the procedure duration and downloaded at the end of each procedure. The methodology for using these dosimeters has been previously described(171). The dosimeter is plugged into a personal computer

(PC) to be read using the Instadose^{TM} software. The readout from the PC demonstrates the air kerma incident on the dosimeter with a conversion calculation to give the personal dose equivalent $H_p(10)$. $H_p(10)$ (the dose equivalent in soft tissue measured at a depth of 10mm) is an accepted surrogate measurement of effective dose (*E*). This is inaccurate in this setting, as the operator wears a lead apron so this value was divided by 21 - in line with the methodology outlined in the NCRP 168 document(172) to give an effective dose (*E*) whilst wearing a lead apron.

Operators were all cardiologists with varying experience. For analysis, they were grouped into three experience categories: Group1 = Registrar, Group 2 = Interventional fellow, Group 3 = Consultant.

Data integrity and statistical analysis:

Data for procedures where an IDD was worn were compared to those procedures where the IDD was not worn to ensure a comparable data set. The continuous outcome measures (OD and P_{KA}) were categorised to form binary measures for use in analysis. For each variable, values below the 75th percentile were included in the reference category and values at or above the 75th percentile were included in the high dose comparison category.

The distributions of variables were assessed. Means and standard deviations (SD) or medians and inter-quartile ranges were used to describe continuous variables, with Mann-Whitney U tests or Kruskal Wallis tests used to compare groups. Categorical variables were compared using a Chi squared test. Significant categorical variables from the Chi – square analysis with a p-value of <0.1 with univariate analysis were included in multivariate logistic regression modelling. Stepwise removal of variables with the highest p-value was performed. In the final model all variables remained significantly associated with the outcome at the 0.05 level.

Results

The study population comprised 3860 patients. The mean age for patients was 66 (SD 13) years. P_{KA} measurements were available for all 3860 procedures and the IDD was worn during 2591 (67.1%) of these procedures. Primary operator dose (OD) was measured in this subset. The cut point for the 75th percentile value for P_{KA} was 61.4 Gycm^2 **(table 3.1).** Procedures above this were considered High P_{KA}. The cut point for the 75th percentile for Operator 1 dose (OD) was 1.90 μSv, with dosimeter readings above this value categorised as high.

All patient and radiation parameters did not differ significantly between procedures where the IDD was and was not worn. Overall and procedure group comparisons for each of the 10 examination categories are given in **table 3.1**. The CORS –LV/AO category was the most numerous, accounting for 1745 (45%) of the procedures performed. The medians of all variables differed significantly across procedural categories. Patients in the TAVI-WU category were the eldest (median 82 years) but the CORS-PA category demonstrated the highest FT (13 (10.4-17.9) mins), K_{AR} (1327 (885-1796) mGy), P_{KA} (99.69 (67.66-160.07)) Gycm^2) and DA (19 (17-22). However, this category accounted for only 0.3% of procedures performed. Median OD was 0.95μSv (Inter quartile range (IQR) 0.00-1.90) and varied significantly across procedure categories (p=0.002) and is demonstrated graphically in **figure 3.1**. Median patient and operator dose for each category within each variable that may impact on radiation dose is given in **table 3.2**.

Table 3. 1 - Overall patient and radiation data and comparisons across procedure categories

	Procedure category											
	Overall	AFA	CORS	CORS-LV/AO	CORS-LHC/RHC	CORS-OCT/IVUS/FFR	CORS-PA	CORS-GRAFTS	PA	RHC	TAVI -WU	p-value
N=	3680	11	1019	1745	200	268	10	413	18	55	121	-
Patient measures												
Age (Years)	66 ±13	77 (72-82)	67 (57-75)	65 (56-72)	69 (54-77)	68 (61-75)	64 (59-67)	72 (66-79)	52 (36-67)	59 (41-72)	82 (78-86)	<0.001
BMI kg/m^2	29.3 (25.5-33.6)	30.5 (25.7-34.8)	29.3 (25.4-33.8)	29.6 (25.7-33.9)	27.9 (24.1-33.3)	29.4 (26.0-33.2)	29.8 (28.3-35.3)	28.9 (25.9-32.9)	25.6 (22.2-30.0)	27.6 (21.2-31.6)	27.7 (24.9-31.4)	<0.001
Radiation measures												
FT (mins)	4.7 (2.9-8.3)	4.5 (1.3-7.7)	3.9 (2.5-6.4)	3.7 (2.6-5.6)	8.1 (5.1-11.9)	9.1 (6.5-12.9)	13.0 (10.4-17.9)	9.8 (6.7-14.4)	10.5 (8.5-14.3)	4.7 (2.0-9.5)	7.5 (4.5-9.7)	<0.001
K_{AR} (mGy)	646 (399-980)	139.0 (32.6-451)	626.0 (398-934)	593.0 (374-872)	613.0 (372-900.5)	841.5 (493.5-1242.5)	1327.0 (885-1796)	1018.0 (665-1476)	391.5 (200-610)	53.8 (19-105)	721.0 (449.0-1124)	<0.001
P_{KA} (Gycm^2)	40.0 (24.8-61.4)	12.93 (3.13-42.70)	37.37 (23.96-56.41)	35.76 (22.89-53.49)	43.25 (26.69-65.28)	49.37 (30.44-72.72)	99.69 (67.66-160.07)	67.11 (43.75-95.58)	34.30 (17.13-57.43)	5.72 (2.24-13.97)	47.86 (32.09-78.38)	<0.001
DA	10 (9-13)	4 (2-9)	9 (8-11)	10 (10-12)	10 (8-12)	12 (9-14)	19 (17-22)	17 (14-20)	8 (5-9)	0 (0-1)	14 (12-16)	<0.001

Footnote: Table shows how the different patient characteristics and radiation measures compare across procedure category. Median and inter-quartile ranges are shown with p-values calculated using Kruskal-Wallis tests. (BMI = body mass index, CORS=coronary angiogram, DA= digital acquisitions, FT=fluoroscopy time, K_{AR} = air Kerma at the interventional reference point, P_{KA} = Kerma area product, TAVI = transcatheter aortic valve implant. AFA = Abdominal/Femoral angiogram only, CORS = Coronary angiography only, CORS-LV/AO = Coronary angiography + aortogram/ left ventriculogram, CORS-LHC/RHC = Coronary angiography + left heart catheterisation + Right heart catheterisation, CORS-OCT/IVUS/FFR = coronary angiography + additional coronary artery lesion assessment with intravascular ultrasound (IVUS), optical coherence tomography (OCT) of fractional flow reserve (FFR), CORS-PA = Coronary angiography + pulmonary angiography CORS-GRAFTS = Coronary angiography + coronary artery bypass graft angiography, PA = Pulmonary angiography alone, RHC = Right heart catheterisation +/- venography , TAVI-WU = Work-up for transcatheter aortic valve implant).

Table 3. 2 - Median radiation dose for patients and operators within variable categories.

Item	P_{KA} ($Gycm^2$)	p-value	OD (μSv)	p-value
N=	3860		2591	
Access		<0.001		0.002
Radial access	38.37 (24.55-57.24)		0.95 (0.00-1.90)	
Femoral access	46.04 (26.17- 72.57)		0.95 (0.00-1.90)	
Jugular access	2.86 (1.43-6.06)		0.72 (0.24-1.19)	
Gender		<0.001		<0.001
Female	27.52 (16.65-44.57)		0.95 (0.00-1.43)	
Male	47.45 (32.22-70.71)		0.95 (0.00-2.38)	
Imaging technique		<0.001		<0.001
Biplane Imaging	58.16 (35.55-89.74)		1.43 (0.00-2.38)	
Single plane	36.44 (22.88-55.27)		0.95 (0.00-1.90)	
Cath lab used		<0.001		0.372
Cath lab 1	37.40 (23.29-59.83)		0.95 (0.00-1.90)	
Cath lab 2	42.49 (26.40-63.97)		0.95 (0.00-1.90)	
BMI category		<0.001		<0.001
BMI >30	53.63 (37.52-76.01)		1.43 (0.00-2.38)	
BMI 25-30	35.96 (24.29-53.02)		0.95 (0.00-1.90)	
BMI <25	21.73 (13.43-33.83)		0.48 (0.00-1.43)	
Operator 1 experience		0.001		0.380
OP1 exp. (Consultant)	38.06 (23.91-60.40)		0.95 (0.00-1.90)	
OP1 exp. (Fellow)	41.11 (25.07-61.37)		0.95 (0.00-1.90)	
OP1 exp. (Registrar)	44.60 (28.38-65.41)		0.95 (0.00-1.90)	
Operator 2 experience		0.825		0.056
OP2 exp. (Consultant)	46.74 (30.65-71.07)		0.95 (0.00-2.38)	
OP2 exp. (Fellow)	45.68 (26.77-67.13)		0.95 (0.00-1.90)	
OP2 exp. (Registrar)	44.76 (29.50-69.86)		1.43 (0.48-2.86)	

Footnote: This table demonstrates the differences in median (IQR) radiation dose values for the patient ($Gycm^2$) and operator (uSv) between categories within each variable measured. (BMI = Body mass index, OD = primary operator dose, OP1= operator 1 OP2 = operator 2).

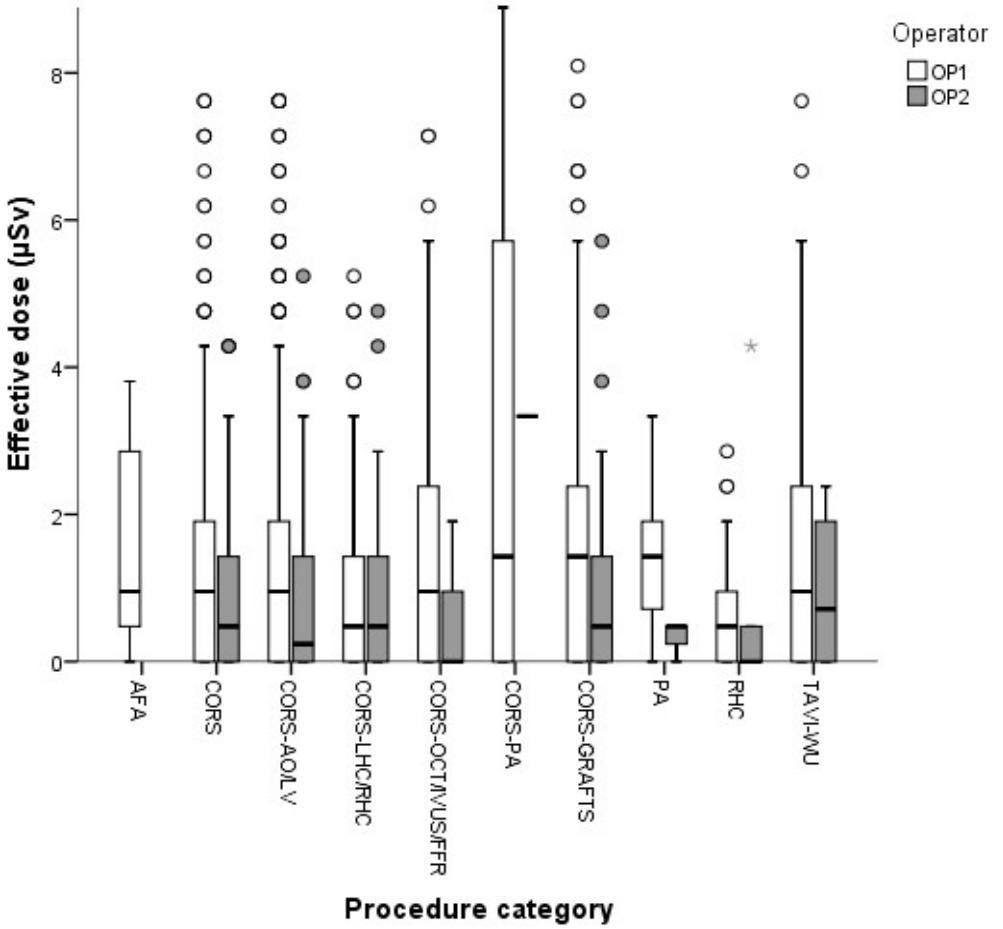

Figure 3. 1 - Median radiation dose to operators by procedure category.

Legend: This graph demonstrates the differences in operator dose accross procedure categories. (AFA = Abdominal/Femoral angiogram only, BMI = body mass index, CORS = Coronary angiography only, CORS-LV/AO = Coronary angiography + aortogram/ left ventriculogram, CORS-LHC/RHC = Coronary angiography + left heart catheterisation + Right heart catheterisation, CORS-OCT/IVUS/FFR = coronary angiography + additional coronary artery lesion assessment with intravascular ultrasound (IVUS), optical coherence tomography (OCT) of fractional flow reserve (FFR), CORS-PA = Coronary angiography + pulmonary angiography CORS-GRAFTS = Coronary angiography + coronary artery bypass graft angiography, OP1 = operator 1, OP2 = operator 2, PA = Pulmonary angiography alone, RHC = Right heart catheterisation +/- venography , TAVI-WU = Work-up for transcatheter aortic valve implant: Includes coronary angiography, aortography, ilio-femoral angiography).

Factors contributing to a high P_{KA}

Overall, 64% of patients were male, 33% of patients were overweight (BMI 25-30) and 45% were obese (BMI>30). Under univariate analysis, the CORS-PA procedure category demonstrated the highest odds ratio (OR), with these patients having a 16 fold greater chance of receiving a high dose in comparison to the CORS baseline category.

Under multivariate analysis, a BMI>30 was the strongest predictor for a high P_{KA}, demonstrating that after correcting for all other variables in the model, these patients were 19.1 times more likely to receive a high dose. Males were more likely to be in the highest quartile of radiation dose (OR: 5.3, 95% CI: 4.3 - 6.7), compared to females and Biplane imaging was also more likely to be associated with a high P_{KA} (OR=5.2 (95%CI: 4.2 - 6.5)) **(table 3.3).**

Factors contributing to a high operator 1 dose (OD)

In the subset of 2591 patients where the IDD was worn by operators, patients were predominantly male (64%), 33% were overweight and 46% were obese. Biplane imaging was used in 21% of cases and radial access was used in 69% of procedures. Under univariate analysis, a BMI >30 was demonstrated to be the strongest predictor of a high OD, with an OR of 3.3 (95%CI: 2.5 - 4.4). This effect persisted in the multivariate model, where after correcting for all other variables in the model, a BMI >30 was the strongest predictor of a high OD, (OR = 3.3 (95%CI: 2.4 - 4.4)). Of the 10 procedural categories, TAVI-WU demonstrated the highest OR for predicting a high OD, (OR = 2.7 (95%CI: 1.5 – 4.8)). Males, biplane imaging and radial access were also associated with a high OD **(table 3.4).**

Table 3. 3 - Regression analysis for variables that impact on PKA for diagnostic cardiac angiography procedures.

	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	P value
Gender			<0.001			<0.001
Female	Ref.Cat.			Ref.Cat.		
Male	4.39	3.61-5.32	<0.001	5.34	4.26-6.68	<0.001
Access			<0.001			
Femoral	Ref.Cat.					
Jugular	0.13	0.02-1.00	0.05			
Radial	0.53	0.46-0.62	<0.001			
Cath lab used			<0.001			<0.001
Cath lab 1 used	Ref.Cat.			Ref.Cat.		
Cath lab 2 used	1.20	1.04-1.39	0.01	1.37	1.14-1.64	0.002
Imaging technique			<0.001			<0.001
Single plane	Ref.Cat.			Ref.Cat		
Bi-plane	3.93	3.34-4.62	<0.001	5.17	4.14-6.47	<0.001
BMI			<0.001			<0.001
BMI <25	Ref.Cat.			Ref.Cat		
BMI 25-30	3.58	2.61-4.90	<0.001	3.88	2.74-5.50	<0.001
BMI >30	9.59	7.13-12.90	<0.001	19.08	13.52-26.94	<0.001
Procedure type			<0.001			<0.001
CORS	Ref.Cat.			Ref.Cat		
AFA	0.40	0.05-3.12	0.386	0.25	0.03-2.26	0.215
CORS-LV/AO	0.85	0.70-1.03	0.102	0.88	0.70-1.10	0.254
CORS-OCT/IVUS/FFR	2.55	1.91-3.41	<0.001	3.47	2.46-4.89	<0.001
CORS-PA	16.08	3.39-76.29	<0.001	10.36	1.96-54.77	0.006
CORS-RHC	1.64	1.17-2.31	0.004	2.51	1.66-3.79	<0.001
CORS-GRAFTS	5.15	4.02-6.60	<0.001	3.66	2.70-4.96	<0.001
PA	1.15	0.37-3.53	0.809	1.51	0.40-5.67	0.542
RHC	0.32	0.11-0.88	0.028	0.45	0.15-1.37	0.157
TAVI-WU	2.55	1.72-3.80	<0.001	1.85	1.13-3.01	0.014
Operator 1 Experience			0.077			0.010
Consultant	Ref.Cat.			Ref.Cat.		
Registrar	1.29	1.04-1.61	0.024	1.51	1.15-1.98	0.003
Fellow	1.06	0.90-1.24	0.480	1.06	0.87-1.28	0.588

Table 3.3 cont..

Operator 2 Experience			0.72
Consultant	Ref.Cat.		
Registrar	0.81	0.46-1.42	0.455
Fellow	0.97	0.55-1.73	0.923

Footnote: This table demonstrates the odds ratio and significance for all variables that impact on a high P_{KA} in the study under univariate and multivariate logistic regression. (AFA = Abdominal/Femoral angiogram only, BMI = body mass index, CORS = Coronary angiography only, CORS-LV/AO = Coronary angiography + aortogram/ left ventriculogram, CORS-LHC/RHC = Coronary angiography + left heart catheterisation + Right heart catheterisation, CORS-OCT/IVUS/FFR = coronary angiography + additional coronary artery lesion assessment with intravascular ultrasound (IVUS), optical coherence tomography (OCT) of fractional flow reserve (FFR), CORS-PA = Coronary angiography + pulmonary angiography CORS-GRAFTS = Coronary angiography + coronary artery bypass graft angiography, OP1 = operator 1, OP2 = operator 2, OR = odds ratio PA = Pulmonary angiography alone, Ref.Cat. = reference category, RHC = Right heart catheterisation +/- venography, TAVI-WU = Work-up for transcatheter aortic valve implant: Includes coronary angiography, aortography, ilio-femoral angiography)

Table 3. 4 - Regression analysis for variables that impact on operator dose for diagnostic cardiac angiography procedures.

	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	P value
Gender			<0.001			<0.001
Female	Ref.Cat.			Ref.Cat.		
Male	1.77	1.44-2.17	<0.001	1.66	1.33-2.06	<0.001
Access			0.053			<0.001
Femoral	Ref.Cat.			Ref.Cat.		
Jugular	0.83	0.18-3.84	0.815	1.79	0.26-12.16	0.565
Radial	1.29	1.05-1.58	0.017	2.34	1.69-3.17	<0.001
Cath lab used			0.793			
Cath lab 1 used	Ref.Cat					
Cath lab 2 used	0.98	0.81-1.17	0.793			
Imaging technique			<0.001			<0.001
Single plane	Ref.Cat.			Ref.Cat.		
Bi-plane	1.73	1.40-2.14	<0.001	2.18	1.68-2.84	<0.001
BMI			<0.001			<0.001
BMI <25	Ref.Cat.			Ref.Cat.		
BMI 25-30	1.66	1.22-2.27	0.001	1.51	1.09-2.08	0.011
BMI >30	3.31	2.49-4.41	<0.001	3.25	2.42-4.37	<0.001
Procedure type			0.011			0.014
CORS	Ref.Cat.			Ref.Cat.		
AFA	1.94	0.35-10.68	0.448	3.13	0.50-19.57	0.223
CORS-LV/AO	1.03	0.82-1.30	0.793	0.97	0.77-1.24	0.818
CORS-OCT/IVUS/FFR	1.41	0.97-2.05	0.069	1.44	0.98-2.12	0.067
CORS-PA	1.94	0.48-7.84	0.354	1.87	0.43-8.03	0.404
CORS-RHC	0.83	0.50-1.36	0.454	1.28	0.74-2.20	0.376
CORS-GRAFTS	1.53	1.11-2.12	0.010	1.86	1.24-2.79	0.003
PA	0.86	0.18-4.03	0.849	1.49	0.28-7.88	0.641
RHC	0.52	0.18-1.49	0.222	0.91	0.24-3.36	0.882
TAVI-WU	2.05	1.24-3.39	0.005	2.68	1.50-4.76	0.001
Operator 1 Experience			0.094			
Consultant	Ref.Cat					
Registrar	1.00	0.74-1.34	1.000			
Fellow	1.23	0.92-1.65	0.168			

Table 3.4 cont..

Operator 2 Experience			0.190
Consultant	Ref.Cat		
Registrar	0.76	0.41-1.42	0.391
Fellow	1.35	0.76-2.40	0.310

Footnote: This table demonstrates the odds ratio and significance for all variables that impact on a high OD in the study under univariate and multivariate logistic regression. (AFA = Abdominal/Femoral angiogram only, BMI = body mass index, CORS = Coronary angiography only, CORS-LV/AO = Coronary angiography + aortogram/ left ventriculogram, CORS-LHC/RHC = Coronary angiography + left heart catheterisation + Right heart catheterisation, CORS-OCT/IVUS/FFR = coronary angiography + additional coronary artery lesion assessment with intravascular ultrasound (IVUS), optical coherence tomography (OCT) of fractional flow reserve (FFR), CORS-PA = Coronary angiography + pulmonary angiography CORS-GRAFTS = Coronary angiography + coronary artery bypass graft angiography, OP1 = operator 1, OP2 = operator 2, OR = odds ratio PA = Pulmonary angiography alone, Ref.Cat. = reference category, RHC = Right heart catheterisation +/- venography , TAVI-WU = Work-up for transcatheter aortic valve implant: Includes coronary angiography, aortography, ilio-femoral angiography).

Discussion

This study is a large and comprehensive analysis of factors that can impact on patient and operator radiation dose during 10 different diagnostic cardiac procedures performed in a tertiary cardiac catheter laboratory over 16 month period. There was no significant difference between the radiation dose variables when an IDD was or was not worn and this is important when establishing results for operator dose and whether they are relevant across the entire cohort.

A local, multicentre diagnostic reference level (DRL) for CA was developed in 2013 and published in 2014.(166) The 75th percentile of 61.4 Gycm^2 in this study appears to be similar to that studies' DRL for CA of 58.65 Gycm^2 and importantly, the median P_{KA} value appears to be lower than that studies' 75th percentile DRL.(166) This demonstrates ongoing compliance with the local DRL, even with the addition of more complex procedures that were not included in the DRL study of 2014.

Obesity

The multivariate analysis demonstrates that after correcting for all other variables in the model, risk of exposure to high P_{KA} and OD values was highest in obese patients. This is consistent with previous research where obesity was demonstrated to significantly increase the radiation dose used during coronary angiography.(54) However, the present study supplements these findings with the additional information that a high patient BMI is the strongest predictor for both a high patient and operator dose across a range of diagnostic procedures. A high patient BMI means a greater patient thickness which requires more X-ray tube output. The X-ray system boosts exposure automatically but increases patient dose from the increased absorption and scatter of X-rays from the additional thickness. The additional scatter in turn increases OD.

Catheter access route

Radial arterial access has previously been demonstrated to be a procedural factor that increases P_{KA}(173-175) and operator dose.(43,75) However, in the present study, under multivariate analysis, access route did not remain significantly associated with a high P_{KA} at the 5% level. However, radial artery access was associated with a high OD. This is important as radial artery access is now the access route of choice, with lower vascular complication rates(41,42) and a higher patient preference.(41) This study shows a predominantly radial approach and operators are familiar with the technique. The reason for a higher OD with radial access is likely due to the operator standing closer to the radiation source and this observation has previously been highlighted as a possible reason for a higher OD.(47,173)

Biplane imaging

Unsurprisingly, biplane imaging was demonstrated to significantly increase high P_{KA} and OD rates. Biplane imaging uses an additional C-arm and X-ray source to acquire images and it has previously been demonstrated to increase FT, DA(176) and P_{KA}.(56) The study by Lin et al also demonstrated that imaging of saphenous vein grafts and patient gender impact on P_{KA},(56) a finding that is has been replicated in this study, where the CORS-GRAFTS procedure category was demonstrated to be associated with a high P_{KA} and OD under univariate and multivariate analysis. Biplane imaging takes more images and may increase magnification, as it requires the anatomy to be placed in the isocentre of the image in both planes, positioning the patient closer to the X-ray source, which will increase skin dose. In addition, biplane imaging may increase the air-gap between the patient and

the detector, increasing the incident air Kerma. These factors will also impact on OD and the ceiling suspended lead shield may be more difficult to position in order to protect the operator from the additional radiation from the two C-arms.

X-ray system used

It is interesting that one X-ray system delivered more P_{KA} than the other and that this was a significant predictor under multivariate analysis for a high P_{KA}. This did not, however, equate to a high OD. Both systems were identical models of the same age and used the same imaging protocols and exposure parameters. One explanation for this finding may be a difference in dose area product meter (DAP meter) readings between the two systems. Median P_{KA} varied only slightly between the systems. Both systems were tested on a regular basis for dose outputs and the accuracy of the DAP meter, and there are acceptable error ranges for DAP meters. Others studies suggest that an error of ±25% is usually deemed acceptable,(19,22) which is far greater than the difference seen here.

Procedural Categories

Coronary angiography (CORS) was used as the baseline/reference procedure category for this study and the other categories were compared against this. CORS is seen as the baseline procedure of cardiac angiography, with most other procedure categories building on it. CORS and CORS-AO/LV account for 71.6% of procedures in this study. Only AFA, PA and RHC procedures did not include coronary angiography.

It is unsurprising therefore that those procedure categories that built on the CORS reference procedure, demonstrated a higher P_{KA}. Of the procedure categories, CORS with pulmonary angiography (CORS-PA) was the strongest procedural predictor for a high P_{KA}. CORS-PA had the highest median P_{KA} and DA count. CORS-PA routinely uses bi-plane angiography, in which the planes are used in the posterior-anterior projection and lateral projection for the PA component. The lateral projection is very steep and steep or more extreme angles have been shown to increase P_{KA}.(177)

Intra coronary assessment of coronary artery disease with the use of pressure wires (FFR) and intra-vascular imaging with OCT or IVUS is also shown to impact on $P_{KA,}$ although it did not reach significance for a high OD. The results here show that these additional assessment tools increase the FT, P_{KA} and DA for diagnostic procedures. FFR is recommended in the assessment of intermediate lesions prior to revascularisation(178)

and the use of these additional tools may increase over time so it is therefore important to measure their impact on radiation dose.

Operator Experience

Operator experience is shown to impact on P_{KA} during CA under multivariate analysis. After correcting for other variables, the least experienced operators (registrars) were statistically more likely to deliver high P_{KA} values and these findings complement those of the REVERE trial where less experienced radial access operators delivered a higher P_{KA}.(170) The higher P_{KA} seen is possibly due to increased fluoroscopy times when manipulating guide wires and catheters, and possibly a higher number of repeat DA from catheters disengaging mid-acquisition. A higher number of DA and FT for inexperienced operators was also noted in the REVERE trial.(170) Other studies have demonstrated a difference between individual operators in terms of FT, K_{AR} and P_{KA} delivered, though this was not attributed to experience level.(175,179) Operator experience did not appear to impact on OD in this study. All operators had training in the use of radiation and the effective use of protection measures, supplemented through annual refresher training.

Limitations:

While not measured in this study, the effective use of the ceiling suspended shield would make a significant impact on OD and this should be analysed in future studies. Beam kV, mAs and beam geometry were not collected for each procedure, given the cohort size and this could have impacted on dose for different procedures.

Conclusions

This study demonstrates that radiation dose to patients and the operator performing the procedure is multifactorial and is affected by both patient and procedure related variables. Some variables impact on radiation dose more than others and some variables are predictive of a high P_{KA}, some predictive of a high OD, and some both. Overall, a high patient BMI is the strongest predictor for both a high patient and operator radiation dose.

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cardiac scientists and cardiologists for their assistance in the data collection and participation in this study.

Current implications

This study was published in 2019. As such it is very current and contemporary.

Chapter 4 -

Incorporated as Chapter 4:

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Details of my contribution to authorship:

I wrote the research study outline and protocol after reviewing current literature. I designed the study in consultation with local experts (co-authors). I performed a literature review of all relevant, previously published material and reviewed current guidelines. I sought and obtained ethical committee approval. I led the collection of relevant data.

I analysed the data obtained, performed calculations and statistical analysis. I continued consultation with local experts in the field (co-authors) and as lead author, wrote up the findings before sending out the manuscript for critical review by the co-authors. I liaised with the relevant journal for publication as corresponding author and made suggested changes in line with peer review.

Prologue

In the previous chapter factors that contribute to high doses for the patient and the primary operator were investigated. Percutaneous intervention for structural pathology of the heart requires a larger team than for angiography. During these newer, more contemporary and complex procedures, occupational radiation dose is not just a concern for the primary operator. The additional staff members may stand close to the patient during these procedures, particularly the anaesthetist and the trans-oesophageal echocardiogram (TOE) operator. The radiation dose to the team for these procedures has had little investigation and chapter 4 set out to fill this void in the literature.

Radiation Exposure of Operators Performing Trans-oesophageal Echocardiography During Percutaneous Structural Cardiac Intervention

Introduction

Percutaneous interventional procedures, guided by fluoroscopy for structural pathology of the heart are now commonplace and procedures such as trans-catheter aortic valve implantation (TAVI) offer an alternative treatment option to open heart surgery (180). These procedures and many others, including left atrial appendage (LAA) occlusion and MitraClip™ implants require guidance with trans-oesophageal echocardiography (TOE) in addition to fluoroscopy (4,82). This exposes the echocardiographer and/or echocardiologist who operate the TOE probe and console to the harmful effects of scattered ionising radiation. Whilst recent publications have highlighted the risks of radiation to the staff performing fluoroscopically guided cardiac procedures (63,64,78), none of these studies were inclusive of radiation dose to TOE operators in this environment.

Primary operators, usually the cardiologist performing the procedure, have tableside and ceiling suspended lead shields in place to protect them from the harmful effects of radiation. These are usually only in place on the right side of the procedure table, where the primary operator and their assistant stand. There is often no specific additional protection installed at the head end or left side of the procedure table where the TOE operator would stand. Recent guidelines have highlighted the risks of radiation to TOE operators and the lack of evidence surrounding radiation dose to TOE operators (83). All staff working in this environment are monitored with optically stimulated luminescent dosimeters (OSL) that are interrogated on a monthly basis. While all staff wear these dosimeters, they do not demonstrate how much radiation dose each staff member may receive on a case by case basis.

With the lack of evidence surrounding this issue, this study sought to measure the radiation dose to TOE operators during percutaneous interventional procedures that require TOE guidance and compare their dose to other members of the multidisciplinary heart team. Secondly, we sought to investigate procedural factors that would impact on total radiation dose and the TOE operator dose. Additional lead shielding was also implemented for the TOE operator and the effectiveness of the shielding solution was measured.

Methodology

This single, tertiary centre, observational study, conducted between September 2014 and November 2015 included all x-ray guided procedures requiring TOE guidance in a single hybrid operating theatre, equipped with a contemporary cardiovascular X-ray system (Siemens Artis Zee ceiling, Siemens Healthcare, Erlangen, Germany).

Four key roles (Primary catheter operator (OP1), secondary catheter operator (OP2), anaesthetist (ANA) and the TOE operator (TOEOP)) who were in attendance wore an instantly downloadable dosimeter (IDD) (Instadose^{TM} Mirion technologies USA) for the duration of each procedure. The IDD was worn on the outside of the lead thyroid protection collar by all key staff, except for the TOEOP, who attached the IDD to the posterior aspect of their left shoulder, so that the dosimeter faced the radiation source.

The IDD is a direct ion storage dosimeter, the basic principles of which are well described in the literature (181-183). The dosimeter is based upon the storage of charge in a non-volatile analogue (MOSFET) memory cell, surrounded by a small volume of air, essentially acting as an ion chamber. When scattered radiation emanating from the patient is incident on the detector, ionisation occurs within the ion chamber, altering the stored charge. This change in charge provides a measure of the air kerma (mGy) incident on the detector. The exposure can then be downloaded by connecting the dosimeter to a computer. The personal dose equivalent $H_p(10)$ (mSv) is then calculated by the application of an appropriate algorithm, by the computer, which takes into consideration the typical photon energy incident on the dosimeter. The IDD has a broad dose and energy response of 0.01mSv – 5 Sv and 5 KeV – 6 MeV respectively (NVLAP lab code 100555-0 for ANSI N13.11-2009 categories IA, IIA, and IIC).

The personal dose equivalent $H_p(d)$ is defined as the dose equivalent in soft tissue below a specified point on the body at an appropriate depth. For penetrating x-rays this depth is 10mm and therefore denoted as $H_p(10)$. $H_p(10)$ is normally considered to provide a conservative or close approximation to effective dose (*E*)(184). However as the IDD was located outside the protective apron, $H_p(10)$ in this case would significantly overestimate effective dose. The results in $H_p(10)$ were therefore converted to effective dose, by dividing the value by 21, in line with the methodology outlined in the NCRP 168 document (172). This conversion allows for the dose across key staff to be compared along and with other studies.

Radiation protection

All personnel working in the hybrid theatre wore a lead apron or apron and skirt with a minimum of 0.25mm of lead equivalent properties at the back and 0.5 mm at the front. A collar for thyroid protection was also worn. In addition, there was the option for staff to wear a lead lined theatre hat and lead goggles with lead equivalent properties of 0.5 mm. OP1 and OP2 stood on the patient's right side for all procedures, with the exception of surgical access TAVI procedures, where OP1 stood either on the patients' left side (trans apical access TAVI) or at the head of the procedure table (trans aortic TAVI procedures). OP1 and OP2 were protected by a table mounted lower body radiation lead shield (skirt), with 1mm lead equivalent properties and when standing on the patient's right side, a ceiling mounted "drop down" lead Perspex shield with 0.5mm lead equivalent properties. The ANA was positioned at the head of the patient and was provided with a lead Perspex shield on wheels with 1mm lead equivalent properties. The TOEOP was positioned at the head of the patient, toward the patients left side and stood obliquely, predominantly with their back to the x-ray source. The TOEOP had access to use the Perspex shield on wheels but had no other specific additional protection. A plan view of approximate staff and shielding positions is demonstrated in **Figure 4.1**.

Procedural radiation measures collected were:

- Procedure type.
- Fluoroscopy time (FT).
- Total radiation dose (Kerma area product (KAP)).
- Patient body mass index (BMI).
- Patient gender.
- C-arm projection most used during each procedure.

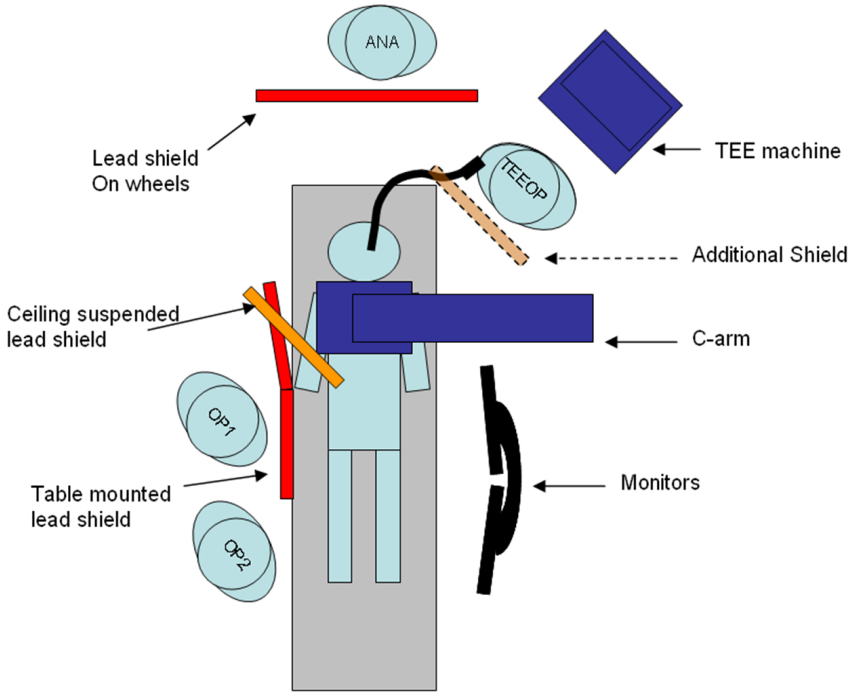

Figure 4. 1 - Graphical representation of approximate positions of key staff members and lead protection apparel.

Legend: This diagram shows the approximate location of the key personnel monitored during structural cardiac intervention procedures and their position relative to the c-arm (X-ray source). It shows the position of lead shield on wheels which was available for the ANA and TOEOP and the position of the table and ceiling suspended shielding for OP1 and OP2. In addition, the position of the additional ceiling suspended shielding is shown, which was implemented for a further 50 procedures (dotted line). (ANA = anaesthetist, OP1 = primary operator, OP2 = secondary operator, TOEOP = Trans-oesophageal echocardiography operator).

Procedures

To aid analysis, procedures were grouped into the following categories:

- Trans-femoral transcatheter aortic valve implant or intervention (TAVITF).
- Transcatheter aortic valve implant or intervention using open surgical access, either trans-aortic or trans-apical (TAVIS).
- Mitral valve intervention (MVI).
- Left atrial device implant (LADI).
- Ventricular or atrial septum intervention/implants (VASI).

Additional protection measures for TOEOP

After reviewing data from the initial procedures, steps were taken to reduce TOEOP dose and an additional ceiling suspended lead Perspex shield with 0.5mm lead equivalent properties (Mavig GmbH, Munich, Germany), identical to that available to OP1 was mounted to the ceiling of the hybrid theatre, such that the TOEOP could use it for additional protection (**Figure 4.2**). With this solution in place, dosimeters were worn for a further 50 procedures and the results from the IDD, worn by the four key roles, compared for procedures before and after the additional protection was installed. Facility human research ethics committee approval was granted for this study.

Figure 4. 2 - Image of the angiography suite with additional ceiling suspended lead shield.

Legend: This image shows the position of the additional ceiling suspended lead shield (arrow) used by the TOE operator for additional protection in the final 50 procedures. It is of the same style as that used by OP1, which is also shown. The authors advocate this typeof shielding to be used for procedures where TOE operators are required on a regular basis.

Analysis

In line with other studies investigating radiation dose levels (166), and international guidelines (7), the Kerma –air –product (KAP) was used as the primary measure for overall radiation dose and patient dose. Effective doses were compared across procedure type and TOEOP individuals. The c-arm projection most used during each procedure were divided into five categories and each key operator effective dose per unit of KAP (*E/*KAP*)* was analysed across these categories. C-arm projection categories were defined as: Steep RAO (> -20^{o} (STRAO)), RAO (-6 ^{o} to -20 ^{o} RAO), PA (-5 ^{o} to +5 ^{o}), LAO (6 ^{o} - 20 ^{o} LAO), Steep LAO (>20^{o} (STLAO)). A Pearson correlation coefficient was used for correlation of TOEOP *E* against the different radiation measures. Categorical data was compared across groups with a Chi – squared or Fishers exact test. Continuous variables were tested for normality and groups were compared using a Mann-Whitney U test or Student's T test as appropriate. Statistical significance across multiple groups was performed using a Kruskal Wallis or ANOVA test as appropriate. Multivariate linear

regression was performed to investigate independent predictors for TOEOP dose from the variables collected. A small constant was added to all TOEOP dose values and natural logarithmic transformations were applied. Scatter plots of continuous predictors by the log-transformed outcomes were examined and KAP was also log-transformed for use in regression modelling. Variables with p-values <0.2 in univariable linear regression models were entered into a multivariable linear regression model. Variables with p-values <0.05 remained in the final model. Regression coefficients were exponentiated to obtain the relative effects of predictors on the outcome variable measured in the original units. SPSS v22 (IBM) was used for analysis.

Results

There were 98 procedures performed prior to the installation of the additional ceiling mounted lead Perspex shield and a further 50 procedures after installation. Overall, patients were 54.7% male with a median BMI of 28.70 (IQR = 24.09-32.64). There was no significant difference in gender for procedures before and after the additional lead protection was installed; (58.2% male vs 48.0% male p=0.240), though there was a difference in patient BMI (29.73 (24.39-33.96) before, 26.26 (23.66-30.84) (p=0.012) after).

Procedures without additional TOE operator protection

Before the additional protection was present, a significant difference in radiation dose across the key roles was demonstrated (p<0.001). Median TOEOP *E* was the highest of the key roles, though not statistically higher than OP1 *E*- 2.62 (IQR = 0.95-4.76) vs 1.91 (0.48-3.81) μSv (p=0.101), but was significantly higher than OP2 *E*- 0.48 (0.00-1.91) μSv (p<0.001)) and ANA *E*- 0.48 (0.00-1.43) μSv (p<0.001)) **(figure 4.3).**

Many of the patient and radiation measures were significantly different across the procedural categories. Median TOEOP *E* was significantly different across procedure groups, with LADI procedures demonstrating the highest *E*at 4.76 (IQR 3.81 -11.91)) μSv and TAVIS the lowest *E* at 0.95 (0.00 -1.91) μSv (p<0.001). A predominantly steep right anterior oblique (STRAO) projection was more likely in LADI procedures (100%) and not used in other procedures, including TAVIS (0%) and TAVITF (0%), (p<0.001) (**Table 4.1**). TOEOP *E* had the strongest correlation with KAP (r=0.547, p<0.001).

Table 4. 1 – Patient, procedural and radiation dose related data for each procedural group for procedures before the additional lead protection for the TOE operator was installed.

Measure	All (N=98)	TAVIS (N=19)	TAVITF (N=33)	LADI (N=14)	MVI (N=24)	VASI (N=8)	p=
Male Gender (N)	57 (58.2%)	11 (57.9%)	18 (54.5%)	10 (71.4%)	15 (62.5%)	3 (37.5%)	0.595
BMI (Kg/m^2)	29.73 (24.39-33.96)	27.89 (23.44-33.54)	29.71 (24.44-35.49)	33.55 (30.49-37.04)	24.89 (21.87-29.19)	35.49 (32.90-43.16)	<0.001
FT (minute)	15.6 (10.2-21.1)	9.1 (7.6-10.5)	17.4 (14.2-20.2)	11.2 (9.4-14.8)	22.3 (17.6-35.45)	13.3 (9.3-15.2)	<0.001
KAP ($Gy.cm^2$)	88.26 (59.63-154.72)	69.66 (46.65-95.70)	143.04 (73.46-200.85)	123.23 (74.51-154.72)	62.89 (38.79-103.99)	113.16 (53.77-172.43)	0.002
STRAO Projection	21 (21.4%)	0 (0%)	0 (0%)	14(100%)	6 (25.0%)	1 (4.8%)	<0.001

Footnote: This table demonstrates the medians (inter-quartile range) for patient and radiation related variables across the different procedure categories prior to the installation of the additional protection shield. (BMI = body mass index, FT = fluoroscopy time, KAP = Kerma air product, STRAO = Steep right anterior oblique,). LADI Left atrial device implant, MVI Mitral valve intervention, TAVITF = Trans-femoral transcatheter aortic valve implant or intervention, TAVIS = Transcatheter aortic valve implant or intervention using open surgical access, either trans-aortic or trans-apical, VASI = Ventricular or atrial septum intervention/implant.

The TOEOP effective dose/KAP (*E*/KAP)composite value, when grouped by predominant c-arm angle demonstrated that doses were higher in procedures where more RAO and steep RAO projections were used (p=0.041) OP1 *E*/KAP was also significantly different across C-arm projections, with the PA projection demonstrating the highest value (p=0.045). *E*/KAP for the other team members *E/*KAP did not differ significantly across c-arm projection categories, OP2 – p=0.856, ANA – p=0.366) (**Figure 4.4**).

There was a large difference in the number of procedures that individual TOE operators performed, ranging from 1 procedure for one operator to 39 procedures for another.

However, there was no statistically significant difference in any patient, procedural or radiation related variable across the individual operators. There was no significant difference in radiation dose to the other key personnel across TOEOP categories.

Impact of additional TOE operator protection

After the additional protection was installed, median TOEOP *E* was reduced by 81.7% - 2.62 (IQR = 0.95-4.76) vs 0.48 (IQR 0.00-1.43) μSv (p<0.001)) (**Figure 3.3)**. Radiation dose to the other key personnel did not change significantly with the installation of the additional protection. All other variables were not significantly different, other than patient BMI and KAP. The procedure numbers across procedure categories were not significantly different after the installation of the additional shielding (p=0.173). The TOEOP *E*/KAP value was significantly lower with the additional protection in place; 28.42 (13.47-52.64) vs 8.40 (0.00-18.53 μSv) p<0.001) (**Table 4.2**).

Univariate and multivariate linear regression demonstrated that the use of the shield was significantly associated with TOEOP radiation dose. A 76% (95% CI 59-86%) (p<0.001) reduction in TOEOP dose is demonstrated in procedures where the shield was in place, compared to those without the shield after correcting for the other variables in the multivariate model. The procedure type was also demonstrated as a significant predictor for TOEOP dose, with LADI procedures demonstrating an 8.7 times greater dose than the reference group: TAVIS (p<0.001). KAP was also demonstrated as a significant predictor (p<0.001).

Table 4. 2 - Impact of the implementation of additional lead shielding for the TOE operator

	No Shield (N = 98)	Shield (N = 50)	p=
Male Gender (N)	57 (58.2%)	24 (48.0%)	0.240
BMI (Kg/m^2)	29.73 (24.39-33.96)	26.26 (23.66-30.84)	0.012
FT (minute)	15.6 (10.2-21.1)	15.9 (10.3-20.8)	0.971
KAP (Gy.cm^2)	88.26 (59.63-154.72)	64.14 (42.68-123.20)	0.048
TOEOP *E*/ KAP ratio) (μSv/Gy.m^2)	28.42 (13.47-52.64)	8.40 (0.00-18.53)	<0.001
STRAO Projection	35 (21.4%)	8 (16%)	0.648
TOEOP *E* (μSv)	2.62 (0.95-4.76)	0.48 (0.00-1.43)	<0.001
OP1 *E* (μSv)	1.90 (0.48-3.81)	2.86 (0.95-4.76)	0.129
OP2 *E* (μSv)	0.48 (0.00-1.90)	0.95 (0.00-2.86)	0.176
ANA *E* (μSv)	0.48 (0.00-1.43)	0.00 (0.00-1.43)	0.559
Procedure type			0.173
TAVIS (N)%	19 (19.4%)	9 (18%)	
TAVITF (N)%	33 (33.7%)	25 (50%)	
LADI (N)%	14 (14.3%)	2 (4%)	
MVI (N)%	24 (24.5%)	12 (24%)	
VASI (N)%	8 (8.2%)	2 (4%)	

Footnote: This table compares the different patient and radiation measures before and after the installation of additional radiation shielding for the TOEOP. All values are median (inter-quartile range). (ANA = anaesthetist, BMI = body mass index, FT = fluoroscopy time, KAP = Kerma air product, LAO = left anterior oblique , OP1 = primary operator, OP2 = secondary operator, STRAO = steep right anterior oblique, TOEOP = trans-oesophageal echocardiography operator, LADI Left atrial device implant, MVI Mitral valve intervention, TAVITF = Trans-femoral transcatheter aortic valve implant or intervention, TAVIS = Transcatheter aortic valve implant or intervention using open surgical access, either trans-aortic or trans-apical, VASI = Ventricular or atrial septum intervention/implant).

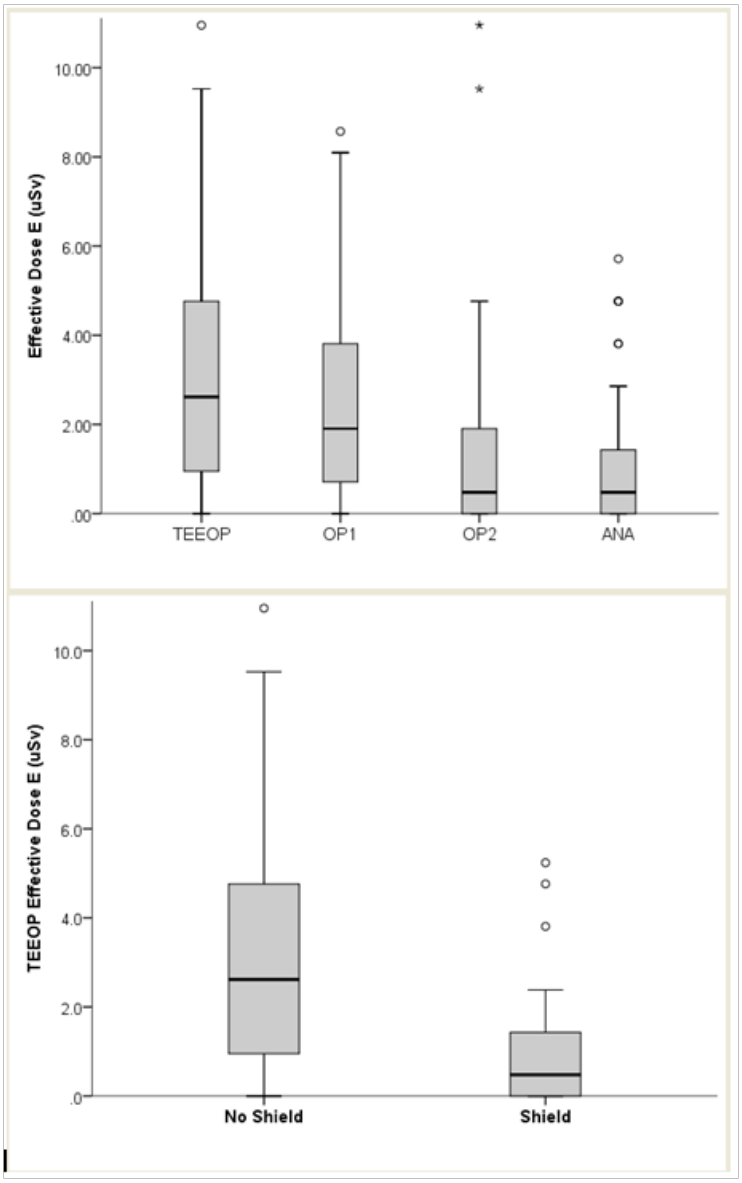

Figure 4. 3 - Radiation dose to TOE operators compared to the rest of the team and the impact of additional radiation protection.

Legend: Radiation dose to the TOE operator is relatively high per procedure when compared to the rest of the attending team (a) but can be reduced by 82% by installing additional ceiling suspended lead protection (b). (ANA = anaesthetist, OP1 = primary operator, OP2 = secondary operator, TOEOP = Trans-oesophageal echocardiography operator).

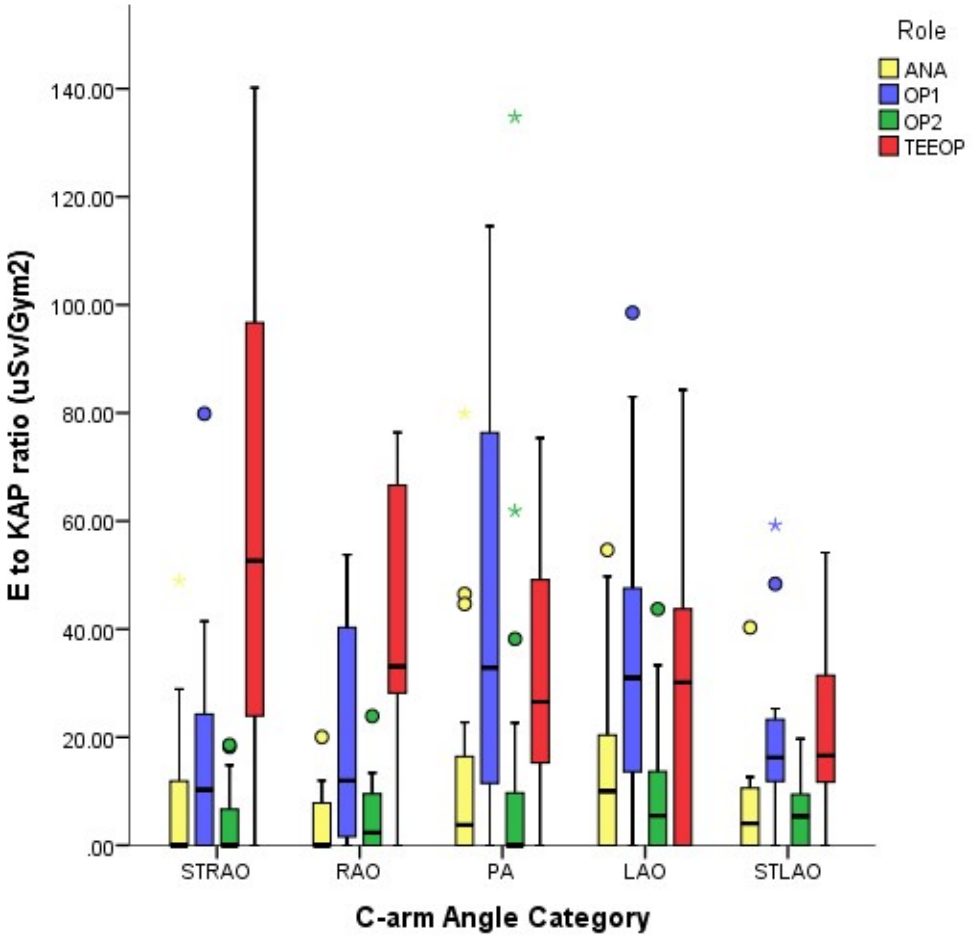

Figure 4. 4 - Operator effective dose /KAP composite measure grouped by C-arm projection.

Legend: This box plot maps the significant incremental increase in TOE operator radiation effective dose per unit of KAP (E/KAP) from the steep LAO projection through to the steep RAO projection (p=0.041), before the additional shielding was in place. OP1 also demonstrated a significant difference in effective dose (0.045). The other key personnel monitored did not demonstrate a significant difference across c-arm categories. It highlights the need for TOE operators to be vigilant with their position relative to the c-arm in procedures with predominantly RAO projections. (ANA = anaesthetist, KAP= Kerma area product, OP1 = primary operator, OP2 = secondary operator, LAO = left anterior oblique, PA = posterior anterior, RAO = right anterior oblique, STLAO = steep left anterior oblique, STRAO = steep right anterior oblique, TOEOP = Trans-oesophageal echocardiography operator).

Discussion

These results demonstrate that before the additional ceiling suspended protection was in place, there was a significant radiation dose to the TOE operator for structural intervention procedures requiring TOE support. The dose is at least as high as the dose to the primary operator, with the associated risks from radiation. Radiation dose to primary operators performing percutaneous cardiac procedures have been associated with cataracts (78) and higher rates of orthopaedic illness and cancer (64). Other studies have also found a higher incidence in left sided brain tumours in physicians performing cardiac procedures (63). The American Society of Echocardiography issued guidelines in 2014 in an effort to highlight the radiation risks associated with percutaneous structural intervention procedures and ways to reduce that risk, including additional shielding. It too highlighted the paucity of data on this important topic (83). There is good data for radiation dose to operators during coronary angiography and intervention (43,67) and additional protection measures have proved to be effective in reducing radiation exposure (185). However, to date there is no data with regard to radiation dose to TOE operators assisting with these procedures.

Drews et al investigated radiation dose to key personnel during surgical TAVI procedures with a mean KAP of 86.61 $Gycm^2$, similar to the 88.26 $Gycm^2$ median overall KAP in this study. They reported a mean *E* of 17.5μSv for the anaesthetist/TOE operator, compared to a median *E* of 2.62μSv for the TOEOP in the present study. However, in that study, the anaesthetist performed the echocardiography, which is a different model to the dedicated TOE operator seen in the present study. In addition, their methodology in calculating effective dose also differed (85).

The dose to the primary operator can also be compared. The median OP1 *E* of 1.9 μSv in the present study appears similar to the 2.3 μSv and 1.2 μSv of the radial and femoral access arms, respectively, of another study investigating operator radiation dose during acute myocardial infarction intervention (67). Again, however, a slightly different method to calculate *E* was used*,* as *E* cannot be directly measured.

At this centre, the TOEOP face their back to the radiation source, thereby potentially lowering the effectiveness of the lead garment. As such, TOE operators should take care to ensure that there is adequate lead equivalent protection in the rear of the lead apron and ‘backless’ style lead aprons should be avoided completely. TOEOP dose was not significantly different between operators, indicating that the high doses seen were not attributed to the working practices of one or two individuals but more likely related to the

close proximity of the TOEOP to the radiation source. Increasing their distance from the source would reduce the dose but this is difficult to achieve whilst operating the TOE probe and the utilization of the lead shield on wheels is ergonomically challenging.

Procedures with increasing steepness of RAO c-arm projections are demonstrated in this study to deliver higher doses to the TOEOP. In comparison, the lowest *E*/KAP to the primary operator is seen in procedures with steep RAO projections. This is in agreement with a previous study that demonstrated the lowest operator dose with RAO projections and considerably higher doses from backscatter when LAO projections were used (177). In a similar manner, highest TOEOP *E*/KAP is seen in the present study with increasing steepness of RAO projections, as they are stood on the left side of the patient and are more exposed to the higher backscattered radiation. TOE operators should be mindful of this when performing left atrial and mitral valve procedures, where RAO projections are predominantly used. If it is possible to stand on the patient's right side for these procedures, then this should be considered. Radiation doses to the TOEOP were significantly lower after the implementation of the ceiling suspended shield, however doses to OP1 did not significantly decrease and were higher than the TOEOP when both had ceiling suspended shields present. The higher dose to OP1 is likely due to the shorter distance between the patient and OP1 during procedures and the fact that the shield may have been difficult to use for certain procedures, such as TAVIS, where the PA projection is commonly used and in this study, higher doses are demonstrated.

Normalising the operator's dose to KAP is advantageous as it then accounts for confounding factors that impact on operator dose. KAP is the primary measure for the amount of radiation used for the procedure. It is a measure of the dose output from the X-ray system and the area exposed. KAP was lower for procedures after the installation of the additional protection and is possibly due to the lower patient BMI in that group; however, *E/*KAP was demonstrated to be significantly lower after the installation of the additional protection, indicating that the lower KAP was not the reason for the lower TOEOP doses.

Conclusion

This study highlights a comparatively significant scattered radiation dose to TOE operators during percutaneous structural intervention, with the associated risks involved. The radiation dose is at least as high as that to primary operator and doses are higher for procedures with predominantly RAO c-arm projections. With the additional ceiling-mounted lead protection in place, radiation dose to TOE operators was reduced dramatically. Based on these results, the authors advocate that similar shielding devices should be implemented in cardiac catheterisation theatres and hybrid operating theatres where TOE operators are utilised to facilitate these procedures on a regular basis.

Perspectives

Competency in medical knowledge: TOE operator radiation dose during percutaneous structural intervention is relatively high when compared to other attending staff.

Translational Outlook 1: Radiation dose to TOE operators can be significantly reduced with additional lead shielding. Specifically, the installation of a ceiling mounted lead shield for TOE operators is recommended for all cath labs and hybrid operating rooms where TOE support is required on a regular basis.

Limitations

This was a single centre observational study and the work practices could be unique to this centre and the results could have been affected by this. However, the findings are relevant to all centres performing structural interventions

Current implications

This study was published in 2018 and is very contemporary literature. It has been recently cited (April 2020) by the Society of cardiovascular angiography and intervention (SCAI) in their multi-society position statement. This document outlines the risks of radiation exposure in the cath labs and advocates a culture of increased safety, education and adoption of new technologies.(186)

Chapter 5 -

Incorporated as Chapter 5:

J. Crowhurst, M. Whitby. Lowering fluoroscopy pulse rates to reduce radiation dose during cardiac procedures. *J Med Radiat Sci*. 65 (2018) 247–249.

Details of my contribution to authorship:

I was contacted by the relevant journal for this editorial. I performed a literature review of all relevant, previously published material and reviewed current guidelines. I analysed the relevant publication content. As lead author, wrote the manuscript before sending out for critical review by the co-author. I liaised with the relevant journal for publication as corresponding author and made suggested changes in line with editorial review.

Prologue

In the previous chapter, radiation dose to the team performing structural intervention was investigated, with the finding that the TOE operator received the highest dose of the team. Additional shielding was used to reduce the dose but there are other ways to reduce radiation dose during these procedures. The previous chapter, discussed the relationship between radiation dose output from the X-ray system and staff dose. The next chapter is an editorial written on request for the *Journal of Medical Radiation science* that discusses radiation dose reduction, with a particular focus on fluoroscopy pulse rate reduction.

Lowering Fluoroscopy pulse rates to reduce radiation dose during cardiac procedures.

Radiation dose to patients undergoing cardiac imaging procedures in cardiac catheterization laboratories (cath labs) can be relatively high so implementing strategies to reduce dose should be a priority for radiation practitioners and catheter operators when working in this environment. Radiation dose to patients should be kept as low as reasonably achievable (ALARA principle) and during cardiac procedures utilizing fluoroscopy, radiation dose parameters including fluoroscopy time, accumulated air kerma (at the reference point, $K_{a,r}$) and air kerma area product ($P_{k,a}$) should be monitored throughout the procedure and recorded in the patient record.(7) The air kerma area product or dose area product (DAP) is an important measure in estimating radiation dose to the patient, as it is a measure of both the incident air kerma and the area of the patient exposed. In addition, the incident air kerma at a reference point from the radiation source is a useful measure in estimating the peak skin dose. Fluoroscopy time (FT) is less indicative of the radiation exposure as it does not capture information regarding the fluoroscopy pulse rate, the dose per pulse and the number of digital acquisitions although it may give an indication of the complexity of the procedure.

There are many ways in which patient dose can be reduced during cardiac procedures, even before optimising the exposure settings of the equipment. These include, using good beam geometry, maintaining a minimal patient to detector distance and keeping the patient as far away from the X-ray tube as possible. Collimating tightly to the area of interest and not overusing electronic magnification is also important. In addition, the inherent advantage of newer systems allow for far greater functionality to adapt default post processing parameters, helping to find the correct balance between image quality and radiation dose for an individual department/ cath lab.

However, one of the easiest ways to reduce dose is to reduce the fluoroscopy pulse rate and/or the digital acquisition frame rate. The advantage of this strategy being that it can be easily adjusted mid-procedure, without interrupting workflow on most modern X-ray systems. Normally, fluoroscopy pulse rates of between 7.5 and 15 pulses per second (PPS) are used for coronary angiography and the choice of pulse rate is dependent on the operator's preference. The publication by Badawy et al in JMRS explores the possibility of using a new image processing protocol and fluoroscopy pulse rates as low as 3 PPS.(33) Their well written retrospective study investigates the impact of reducing the fluoroscopy pulse rate on the total dose area product (DAP) for the procedure. To our knowledge, this is the first study to report pulse rates as low as 3 PPS for coronary angiography. The study reported that a significant reduction in DAP (up to 58%) and $K_{a,r}$ could be achieved by operating as low as 3 PPS, with no significant increase in fluoroscopy time. The authors highlighted the inevitable image quality changes with this approach, such as a reduction in temporal and spatial resolution as well as a degradation of low contrast detectability. However, after a period of adjustment, with appropriate changes made to post processing parameters, such as noise reduction, edge enhancement and temporal filtering, acceptable image quality could be maintained. Though all procedures were successfully completed in the 3 PPS protocol without protocol deviation, only one operator utilized the 3PPS technique. This paper demonstrates that the 3 PPS technique is feasible but future studies investigating this technique should investigate multiple operators using this technique and procedural complication data should be included. This would demonstrate that this technique is safe when being implemented more widely.

Other studies have also investigated reducing fluoroscopy pulse rates for coronary angiography: Abdelaal et al investigated this in a randomized controlled trial in 2014.(29) The study cohort was 363 patients undergoing coronary angiography, with or without ad-

hoc percutaneous coronary intervention (PCI). In their trial, patients were randomised, at a ratio of 1:1 using sealed envelopes to indicate whether their procedure was to be undertaken at either 15 PPS or 7.5 PPS. All X-ray system parameters other than the pulse rate were the same. During diagnostic coronary angiograms, fluoroscopy time was non-significantly different between the groups but DAP was 26% lower in the 7.5 PPS group and interestingly, operator dose saw a 40% relative reduction in the 7.5 PPS group. These results indicate how lower pulse rates can significantly reduce radiation dose to patients and in addition, to the staff performing the procedure.(29) A natural progression of this work is in the optimisation of the digital acquisition (DA) parameters, as DA is used to document the vascular anatomy and is of a higher dose than fluoroscopy. Adjusting DA parameters would also have the potential to contribute to a large reduction in patient and operator dose.

Implications for staff radiation dose

The study by Badawy et al(33) also has implications for the radiation dose to the staff present, particularly the primary operator, who stands closest to the patient during these procedures. Radiation exposure to staff working in cath labs can be significant. Staff that work in this environment have been reported to be at a higher risk of developing certain pathologies, such as skin lesions, cataracts, depression, orthopaedic problems and thyroid disease in comparison to staff that do not work in cath labs(64). Further to these findings, an increase in the risk of skin lesions, hypertension, hypercholesterolemia and cancer across years of working in cath labs was also reported(64). As such, it is important that every effort should be made to reduce radiation exposure during cardiac fluoroscopy procedures. This is especially relevant to those that may spend their entire career working in this environment.

Electrophysiology Procedures

Lowering fluoroscopy pulse rates are also a particularly important dose reduction tool during electrophysiology procedures as electrophysiology procedures perform few digital acquisitions so the majority of the radiation exposure comes from fluoroscopy. Using a modern X-ray system, with low fluoroscopy pulse rates and a low dose per pulse has previously been demonstrated to reduce DAP by over 90%, when compared to an older generation system.(187) That study also tailored the image processing to this low pulse rate and low dose rate protocol. Using a pulse rate of 3 PPS for most electrophysiology procedures has been advocated by the European Heart Rhythm Association (EHRA).(69)

Radiation Safety implications

The paper by Badawy et al(33) in JMRS demonstrates the impact that proactive staff working in the cath lab can have on the radiation exposure of the patient. Using an X-ray system '*straight out of the box'* without some form of customization to the local environment is ill advised. The team using the equipment, including the treating physician, radiographer, medical physicist and equipment manufacturer should optimize the equipment for procedures, depending on its use, which may be different from other sites using the same model. Furthermore, ideally, the X-ray system should be optimized for individual operators, as each will have preferences in terms of image quality (e.g. can tolerate more noise, prefers more edge enhancement).

Fluoroscopy pulse rates, acquisition frame rates and the radiation dose for each pulse can be readily changed on most modern fluoroscopy systems. Further software changes that will enhance the image can also be optimised. In addition, it is important for the team to have multiple options for radiation protocols to suit the needs of the procedure. These protocols should be adjusted during the procedure as required and this should be performed in conjunction with the continuation of good radiation practice, such as optimal beam geometry and adjusting collimation and filtration as necessary. This paper is an excellent example of how exploring imaging options beyond those traditionally used can

reduce radiation exposure to low levels, which is of benefit to the care of the patient and the staff working in this environment. Sensible, iterative changes, where minor, progressive adjustments are made to the imaging protocol can lead to significant patient and staff radiation dose reductions.

Chapter 6 –

J. Crowhurst, H. Haqqani, D. Wright, M. Whitby, A. Lee, J. Betts, R. Denman. Ultra-low radiation dose during electrophysiology procedures using optimized new generation fluoroscopy technology. *Pacing Clin Electrophysiol.* 2017 Aug;40(8):947-954

Details of my contribution to authorship:

I wrote a research study outline and protocol after reviewing current literature. I designed the study in consultation with local experts (co-authors). I performed a literature review of all relevant, previously published material and reviewed current guidelines. I wrote the research protocol and sought and obtained ethical committee approval. I liaised with relevant experts in the field and obtained permission for use of data from relevant stakeholders. I collected the relevant data.

I analysed the data obtained, performed calculations and statistical analysis. I continued consultation with local experts in the field (co-authors) and as lead author, wrote up the findings before sending out the manuscript for critical review by the co-authors. I liaised with the relevant journals for publication as corresponding author and made suggested changes in line with peer review.

Prologue

Chapter 5 discusses radiation dose reduction for cardiac procedures, with a particular focus on fluoroscopy pulse rate reduction in order to reduce dose. With that in mind, chapter 6 focusses on radiation dose reduction during electrophysiology procedures, where particularly long fluoroscopy times may be seen and which have previously been associated with high radiation doses.(86) This chapter describes features of newer generation X-ray systems that allow them to be configured to reduce dose and the dose reductions that can be made. It also puts the magnitude of dose reduction in perspective, with some comparisons to other studies in the literature.

Ultra Low Radiation Dose During Electrophysiology Procedures Using Optimised New Generation Fluoroscopy Technology

Introduction:

Electrophysiology (EP) procedures require catheters to be manipulated accurately inside the heart. Fluoroscopic imaging uses ionising radiation to enable visualisation of the various catheters which are used for recording, pacing, mapping and ablation. Procedures have become increasingly complex in recent years and this is associated with longer fluoroscopy times, resulting in the potential for greater radiation exposure for the patient.(2) Inserting permanent pacemakers (PPM) and internal cardiac defibrillators (ICD) generally require less fluoroscopy than for radiofrequency ablation (RFA) but bi-ventricular devices have been associated with four times the dose of conventional rhythm devices.(188) A recent publication has highlighted the risks of low energy radiation over long periods of time to the operator(64) and the side effects of high radiation doses to the patient, in terms of radiation-induced dermatitis are well recognised.(2)

Cardiovascular fluoroscopy systems have seen considerable advances over the years and can be more readily configured peri-procedurally to tailor the imaging to the needs of the procedure. The number of pulses per second and the dose per pulse can be adjusted mid procedure. Together, these beam properties will affect the overall radiation dose as well as the resulting image quality.

Electroanatomic 3D mapping systems (Carto3 (Biosense Webster, Diamond Bar, CA, USA) and NavX (St Jude Medical MN USA)) and nonfluoroscopic magnetic guidance systems (*Mediguide*™, St Jude Medical, St Paul, MN, USA) have recently emerged as additional technologies that allows catheters to be displayed in real time. The latter uses pre-recorded fluoroscopic loop images and electromagnetic signals, without further use of fluoroscopy.(99) These systems do, however, add additional cost to EP laboratory installations, and ongoing consumable costs by way of catheter purchase.

This study aimed to investigate what radiation dose reductions can be achieved by upgrading from an older image intensifier unit to the latest generation digital fluoroscopy system, optimised to reduce radiation dose but without changing clinical practice. Secondly, we aimed to compare the radiation dose levels obtained with the new system to previously published studies that focused on radiation dose reduction in electrophysiology procedures.

Methods

Radiation dose parameters were prospectively collected for all EP procedures in a single EP laboratory, in a tertiary level institute. The parameters collected were: Patient age, sex, height and weight, the procedure type, fluoroscopy time (FT), dose area product (DAP), the number of digital acquisitions (DA), procedural time (from patient on table to patient off table) (PT) and procedural success (PS). These data were collected between February 2013 and February 2014 when an image intensifier based single plane cardiovascular imaging system (Philips Integris Allura H5000, Philips Healthcare, Einhoven, Netherlands) was used for EP procedures. These same parameters were also prospectively collected between March 2014 and March 2015, when the older system was replaced with the latest generation single plane cardiovascular fluoroscopy system, using a flat panel detector (Siemens Artis Q ceiling, Siemens Healthcare, Erlangen, Germany).

Procedures were separated into seven groups:

- **Devices:** Permanent pacemaker (PPM) and Internal cardiac defibrillator devices (ICD) (including both dual and single chamber).
- **BIV**: Bi ventricular cardiac resynchronisation devices (BIV PPM and BIV ICD).
- **EPS:** Diagnostic electrophysiology studies without ablation
- **RFA**: Radiofrequency ablation (RFA) for supraventricular tachycardia (SVT), atrial flutter (AFL) and AV node/HIS bundle ablation.
- **VAA**: Ventricular arrhythmia (VA) ablation, including focal ablation of premature ventricular ectopics (PVCs), as well as idiopathic and scar related ventricular tachycardia (VT).
- **CAA:** Complex atrial arrhythmia ablation (excluding atrial fibrillation).
- **PVI**: Pulmonary vein isolation for atrial fibrillation.

Equipment settings

All procedures were performed by one of six experienced electrophysiologists, with or without the assistance of a fellow in training. These physicians were all trained and licensed by state authorities in the safe and appropriate use of fluoroscopic equipment and were assisted by a qualified, licensed cardiac radiographer. This team worked together to optimise both radiation dose and image quality throughout the procedures.

With the older system, the fluoroscopy pulse rate was set to 6.25 pulses per second (PPS). Three dose rates were available: low, normal and high, with the system defaulting

to the lowest. This system was used without the stationary grid in place. With the new system, the pulse rate defaulted to 4 PPS and rates could be increased from 4 to 6 to 7.5, 10 or 15 PPS and detector input dose for fluoroscopy could be increased from 6 nGy/ pulse to 12 or 23 nGy/ pulse. This system was used with the stationary grid in place for all procedures. The imaging field was used at 23cm and 25cm field of view respectively and the beam was optimally collimated with both systems to the area of interest, for each phase of each procedure as necessary.

Both imaging systems were checked for image quality and radiation dose compliance on an annual basis by a medical physicist. DAP readings were taken using a calibrated DAP meter housed in the X-ray tube housing. Nominal x-ray dose rates were measured using a calibrated solid state detector (Unfors Xi by Raysafe^{TM}, Billdal, Sweden) on both systems with a 200mm Perspex phantom placed in the beam and a source to detector distance of 700mm.

In addition, the results for each procedure type from this study with the new system were compared to other studies in the literature that focused on radiation dose reduction in electrophysiology procedures.

This study was approved by our institutions Human Research Ethics Committee.

Statistical analysis

Data were assessed for normality with a Shapiro-Wilk (or KS test) and reported as means, standard deviations or medians and interquartile ranges. Student's T test and Mann-Whitney U tests were used for inferential testing as appropriate. Fisher's exact test was used to compare categorical variables. Statistical significance was defined as $p < 0.05$. SPSS V.20 (IBM) was used for analysis of data.

Results:

Typical default fluoroscopy settings and the results of annual testing for both systems are summarised in **Table 6.1**. There are various technical differences between the two systems and dose rate under testing was 87% lower (1.76 vs 0.23 mGy/minute) with the new system.

Table 6. 1 - Default x-ray system fluoroscopy settings- as measured using a 200mm Perspex phantom.

	Old System	New system
Image Field size (cm)	23	25
Fluoro dose rate (mGy/minute)	1.76	0.23
Frame rate (PPS)	6.25	4
X-ray tube voltage (kV)	61	77
X-ray tube current (mA)	7.9	95.1
Pulse width (ms)	10	3.8
Copper filtration (mm)	0	0.9
Stationary Grid used in testing	Yes	Yes

Footnote: This table demonstrates the differences in the default fluoroscopy settings of the 2 x-rays systems used in this study when measured by a solid state detector, with a 200mm perspex phantom. (cm = centimetre, mGy = milliGray, PPS = pulses per second, kV = Kilovolt, mA = milliamp, ms = milliseconds, mm = millimetre)

1537 clinical procedures were included in the study, 776 with the old system and 761 with the new system. Comparisons of patient demographics and radiation dose metrics for each procedure group are given in **table 6.2**. Patient weight was not significantly different between the old and new system cohorts for any of the procedure types. Procedure times were not significantly different between these cohorts, with the exception of the devices group where procedure times were longer with the old system. Fluoroscopy times were similar in all groups with the exception of the devices, BIV and EPS groups, where the times were lower with the new system. Overall, DAP was 91% lower with the new system (from 5.0 (2.0-17.0) to 0.45 (0.16-2.61) $Gycm^2$ ($p>0.001$)) and was significantly lower across all procedure groups with the new system (figure 1). The greatest reduction (93%) was seen in the EPS group (2.0 (1.0-4.5) to 0.14 (0.05-0.41) $Gycm^2$ ($p>0.001$)). Procedural success was not significantly different between the two systems in any of the procedure groups. A comparison of the radiation dose levels from the new system to

previously published studies focusing on radiation dose reduction are presented in **table 6.3**. These results demonstrate that radiation doses with the new system in this study are consistently some of the lowest published in the literature across all procedure groups.

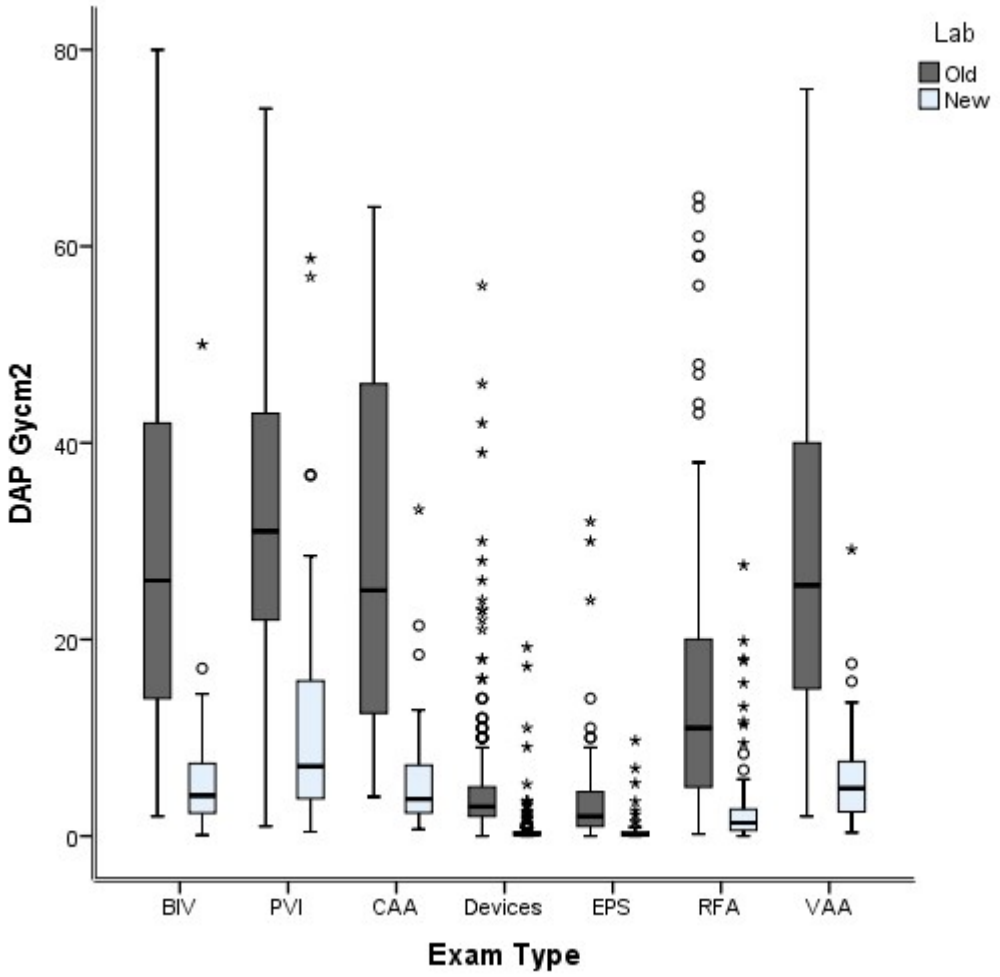

Figure 6. 1 - Box plot graph graphically demonstrating the difference in DAP between the old system and the new system for each procedure type.

Legend: This figure graphically demonstrates the dose reduction between the old system and the new system. (AF = atrial fibrillation, BIV = bi ventricular devices, CAA = complex atrial arrhythmia, DAP = dose area product, Devices = permanent pacemakers and internal cardiac defibrillators, EPS = diagnostic electrophysiology studies, RFA = radio-frequency ablation for simple atrial pathology, VAA = Ventricular arrhythmia ablation).

Table 6. 2 - Patient demographics and procedural comparisons of the two X-Ray systems analysed.

Procedure		N=	Age (years)	Male%	Height (cm)	Weight (Kg)	FT (min)	DAP (Gycm^2)	DA	PT (hr: min)	PS%
Devices	Old	385	74.2 (62.1-81.6)	63.6%	169 (159–177)	80 (65 - 97)	5.3 (3.3 - 8.5)	3.0 (2.0-5.0)	0 (0-0)	1:20 (1:05-1:35)	100%
	New	340	71.4 (61.2-81.2)	62.9%	170 (160–176)	80 (69 – 95)	3.6 (2.4 – 5.9)	0.22 (0.10-0.41)	0 (0-0)	1:12 (1:00-1:30)	100%
	P=		0.094	0.877	0.780	0.458	<0.001	<0.001	0.941	<0.001	1.000
BIV	Old	59	64 (56-73)	81.4%	173(167–178)	94 (77-104)	20.3 (14.8-36.1)	26.0 (13.0-43.0)	4 (2-6)	2:15 (1:50-3:00)	100%
	New	56	63 (57-76)	73.2%	175 (169–180)	87 (75-100)	15.2 (9.9-28.0)	4.1 (2.3–7.4)	2 (1-5)	2:05 (1:40-2:30)	100%
	P=		0.771	0.374	0.302	0.219	0.261	<0.001	0.043	0.388	1.000
EPS	Old	72	51.3 (31.2-67.0)	62.5%	170 (163-177)	83 (70-95)	4.2 (2.0-7.8)	2.0 (1.0-4.5)	0 (0-0)	1:40 (1:20-2:00)	100%
	New	99	41.0 (27.7-56.2)	47.5%	170 (163-179)	78 (66-94)	2.3 (1.3-5.4)	0.14 (0.05-0.41)	0 (0-0)	1:35 (1:20-2:00)	100%
	P=		0.022	0.063	0.961	0.211	0.042	<0.001	0.991	0.956	1.000
RFA	Old	150	52.9 (36.1-64.5)	46.7%	169 (163-177)	81 (67-95)	22.2 (13.2-34.4)	11.0 (5.0-20)	0 (0-2)	2:20 (1:55-2:55)	98.7%
	New	137	52.9 (33.7-66.9)	47.4%	169 (163-176)	80 (65-97)	17.4 (10.5-34.1)	1.34 (0.60-2.71)	0 (0-0)	2:07 (1:45-2:43)	94.2%
	P=		0.767	0.906	0.844	0.896	0.260	<0.001	0.012	0.054	0.052
VAA	Old	46	60.1 (53.2 69.7)	47.7%	169(162-178)	89 (74-102)	39.4 (28.0-48.2)	26 (15-40)	1 (0-3)	4:20 (3.40-4:55)	89.1%
	New	52	58.7 (43.0-69.2)	52.3%	172 (165-177)	86 (74-97)	37.1 (23.5-54.8)	4.85 (2.46-7.59)	0 (0-2)	4:10 (3:15-4:45)	82.7%
	P=		0.840	0.834	0.467	0.492	0.544	<0.001	0.275	0.107	0.271
PVI	Old	45	56.7 (49.4-64.3)	57.8%	173 (165-177)	90 (81-103)	39.7 (34.2-52.1)	31.0 (22.0-43.0)	1 (0-2)	4:35 (4:10-5:10)	88.9%
	New	54	56.1 (44.0-66.5)	77.8%	176 (167-185)	89 (77-108)	42.1 (36.2-52.0)	7.10 (3.83-15.78)	1 (0-2)	4:35 (3:50-5:10)	88.9%
	P=		0.927	0.049	0.148	0.836	0.618	<0.001	0.884	0.983	0.517
CAA	Old	19	40.5 (26.3-66.3)	47.4%	169 (161-174)	70 (59-98)	45.4 (32.4-60.9)	25.0 (12.0-46.0)	0 (0-1)	4:18 (3:50-5:00)	78.9%
	New	23	38.7 (29.9-53.5)	56.5%	173 (164-178)	87 (73-95)	38.7 (29.9-53.5)	3.76 (2.25-7.28)	0 (0-2)	4:00 (3:30-4:30)	87.0%
	P=		1.000	0.757	0.151	0.860	1.000	<0.001	0.243	0.920	0.682

Table 6.2 Footnote: All data are expressed as medians and inter-quartile ranges. (BIV = bi-ventricular devices, CAA = complex atrial ablation. DA= Digital Acquisition**,** EPS = electrophysiology study, FT= Fluoroscopy time, PVI = pulmonary vein isolation, RFA = radiofrequency ablation, PT=Procedural Time, PS= Procedure Success**,** VAA = ventricular arrhythmia ablation).

Table 6. 3 - Comparison of this study to the literature for different categories of procedures.

Study	Procedure type	Guidance system used	Fluoroscopy Time (Minutes)	Dose Area Product ($Gycm^2$)
PPM and ICD implants				
Perisinakis at al 2005(188)	PPM /ICD	N/A	8.2 ± 3.7	11.06 ± 2.80
Perisinakis et al 2005(188)	Bi-V PPM/ ICD	N/A	35.2 ± 21.7	47.65 ± 9.65
Tsapaki et al 2008(86)	PPM	N/A	87 (55-225)	6.7 (1.1–167)
Richter et al 2013(189)	Bi-V	Mediguide™	5.2 (3.0-8.4)	10.7 (6.9 -17.4)
Thibault et al 2015(190)	Bi-V	Mediguide™	6.5 (4.3, 10.7)	7.69 (4.91- 21.82)
Attanasio et al 2016(91)	PPM/ICD/BIV	N/A	13 ± 15	13.72 ± 26.59
Thibault et al 2016(105)	BIV	Mediguide™	5.1 (2.8-9.1)	1.08 (62-229)
This study (New system)	PPM /ICD	N/A	3.6 (2.4 – 5.9)	0.22 (0.10-0.41)
This study (New system)	BIV	N/A	15.2 (9.9-28.0)	4.1 (2.3–7.4)
Simple RFA procedures				
Earley et al 2006(95) (conventional)	RFA (AVNRT, AVRT, flutter)	N/A	13 (2-46)	12 (1-106)
Earley et al 2006(95) (Carto)	RFA (AVNRT, AVRT, flutter)	Carto	6 (1-55)	5 (1-89)
Earley et al 2006(95) (NavX)	RFA (AVNRT, AVRT, flutter)	NavX	4 (0-50)	2 (0-54)
Tsapaki et al 2008(86)	Various RFA	NS	110 (44-420)	83.5 (3-259)
Rogers et al 2010(88)	Simple RFA (AP, AVNRT, Flutter, AVN)	N/A	21.3 ±18.5	8 ±10.3
Vallakati et al 2013(100)	RFA (flutter, AVNRT, WPW, EPS)	Mediguide™	8.25 ±4.9	70.79 ±70.72
Sommer et al 2013(101)	SVT	Mediguide™	0.5 ±1.4	1.87 ±5.54
Lee et al 2014(191)	RFA (AVNRT, WPW, CBT)	N/A	8.8 ±6.9	2.7 ±4.2
Malliet et al 2015(192)	Atrial Flutter	Mediguide™	0.8 (0.4-2.5)	1.61 (0.65-5.37)
This study (New system)	RFA	N/A	17.4 (10.5-34.1)	1.34 (0.60-2.71)

Table 6-3 cont...

AF ablation and VT ablation				
Rogers et al 2010(88)	Complex (AF,VT, CHD)	Carto/NavX	52. 7 ± 23.3	32.8 ±31.7
Dekker et al 2013(107)	AF/atrial/VT ablation	Carto/NavX	24 (IQR=±13)	8.8 (IQR=±8.2)
Sommer et al 2014(193) (last 50 patients in cohort)	AF	Mediguide™	1.1 (0.7–1.5)	4.90 (2.30–6.54)
Malliet et al 2015(192)	AF	Mediguide™	12.5 (7.6-17.4)	11.07 (9.06-20.33)
Schneider et al 2015(90)	AF	Carto /NavX	13.3 ± 8.3	8.37 ± 6.47
Knecht et al 2015(194)	PVI	Carto 3	4.2 (2.6-5.6)	13.2 (6.2-22.2)
Attanasio et al 2017(91)	PVI		13.62 ± 7.11	2.26 ± 2.77
This study (New System)	PVI	Carto 3/ NavX	42.1 (36.2-52.0)	7.10 (3.83-15.78)
This study (New system)	VAA	Carto 3/ NavX	37.1 (23.5-54.8)	4.85 (2.46-7.59)

Footnote: This table demonstrates how the fluoroscopy time and dose area product from the new system in this study compares to other studies in the literature. There are many differences in study methodologies and endpoints with the studies cited. The lowest dose group or the overall dose from each study has been cited as deemed appropriate. DAP data have been converted to $Gycm^2$ for standardisation where necessary. (3^{rd} Q = third quartile, Bi V = bi- ventricular device, AF = atrial fibrillation, AP = accessory pathway, AVN = artioventricular nodal ablation, AVNRT = Atrioventricular nodal re-entry tachycardia, AVRT = Atrioventricular re-entry tachycardia, CBT = concealed bypass tract ablation, CHD = Congenital heart disease, EPS = Electrophysiology study, ICD = Internal cardiac defibrillator, IQR = Inter quartile range, N/A = not applicable, NS = not stated, PPM = Permanent pace maker, PVI= Pulmonary vein isolation, RFA = Radio frequency ablation, VT = Ventricular tachycardia, VAA = ventricular arrhythmia ablation**,** WPW = Wolf Parkinson White).

Discussion

These results demonstrate that very low radiation doses can be achieved with this newer digital imaging system, even with prolonged fluoroscopy times. For example, PPM or ICD device insertions can be performed with a median DAP value of 0.21 $Gycm^2$. This appears comparable to that quoted for a lateral chest x-ray (0.24 $Gycm^2$) in one national audit.(18)

Though it is unsurprising that the newer system achieves a lower dose than the older model, it is the magnitude of reduction (over 90%) that is impressive. The new system used in the study is the vendor's latest model. In order to achieve the low dose rates, the new system's x-ray tube allows greater pre-filtration and shorter pulse widths. This should equate to sharper images and less patient dose. The system was configured by hospital electrophysiologists, technical staff and a medical physicist, in conjunction with the manufacturers' staff in an effort to optimise the image quality during low dose fluoroscopy. There are also image processing options which were optimised at the time of installation. Image processing software is not unique to this vendor. Other vendors have invested in image processing technologies with significant reductions in dose, whilst maintaining image quality, verified in a randomised, controlled trial.(107)

A lower dose per pulse can be used for fluoroscopy, which lowers overall radiation dose but this will reduce image quality. Image quality is not the primary focus for EP procedures. EP catheters are of quite large diameter (4-8mm) and are highly radio-opaque. In most cases, the primary purpose of fluoroscopy is to guide catheters into position, rather than to accurately document anatomy. Lower image quality is therefore acceptable for the majority of procedures. Because of the low dose per pulse and low pulse rate used in this study, long fluoroscopy times are demonstrated in the VAA and PVI ablation groups, when compared to the literature, without this translating to high radiation doses. **Figure 6.2** demonstrates a typical image from the new system used in the study, with the detector input dose set to 6nGy/pulse.

The fluoroscopy pulse rate was also reduced with the new system to a default setting of 4 PPS. This default setting is higher than the 3 PPS advocated by Heidbuchel at al(69) and the 2 PPS in other studies(91,191), indicating that there are further dose savings that could be made.

The systems' settings were consciously optimised peri-procedurally for each procedure and when higher image quality was necessary, such as during transeptal and epicardial

punctures or during placement of left ventricular leads for BIV implants, a higher dose per pulse and/or pulse rate was used but this was reduced again when high image quality was no longer required.

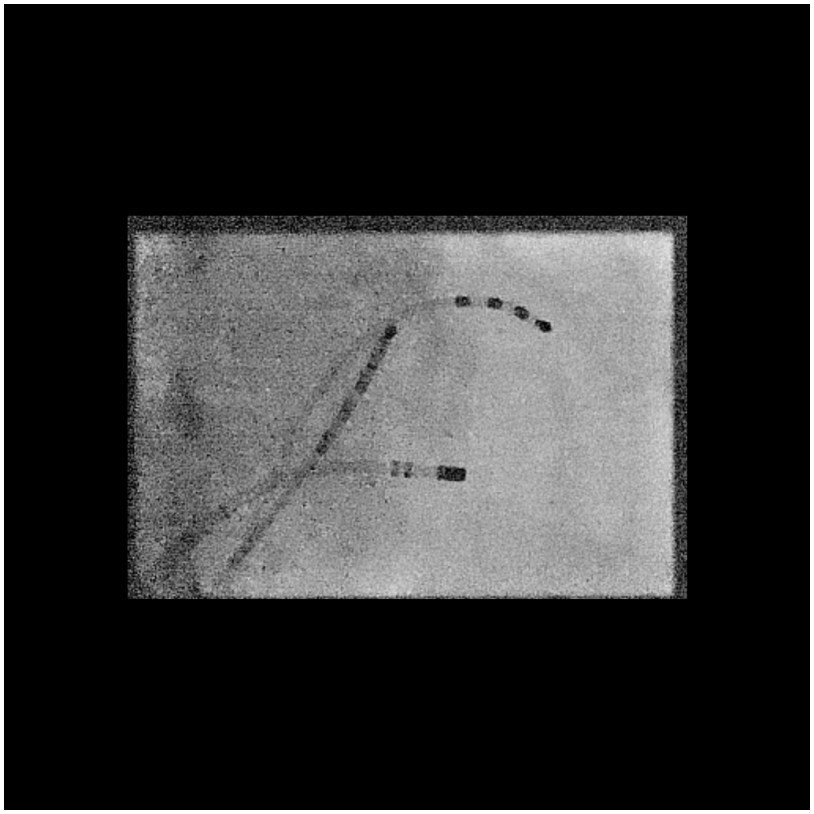

Figure 6. 2 - Example image from the new x-ray system at low dose settings.

Legend: This image shows is a typical example of a still frame produced at the low dose fluoroscopy setting with the new (Siemens Artis Q) x-ray system. The patient was an 87kg female presenting for an AVNRT ablation procedure. It also demonstrates appropriate collimation of the x-ray beam to the area of interest**.**

Beam collimation was also consciously optimised for both systems in this study, which can also reduce DAP as it reduces the area imaged. These combined strategies for dose reduction are not new and have been clearly outlined as dose reduction strategies in the literature.(2,69) It would seem that the ability to lower fluoroscopy dose and pulse rates to these levels is an important factor for dose reduction.

The dose reduction strategies described here with the new system were relatively easy to achieve. The dose per pulse and pulse rates are low but an acceptable image was still produced and procedural success was not compromised as a result. All

electrophysiologists were comfortable with the image quality as a result of the reduced dose and pulse rates. Whilst these strategies have reduced the radiation dose to new levels with this new system, these strategies could be implemented on other contemporary fluoroscopy systems and similar results should be possible.

Removal of the X-ray systems' stationary grid has also been demonstrated to significantly reduce dose(88) and the grid was removed for all procedures with the older unit in this study. The newer system in this study was operated with the stationary grid in place, again demonstrating that there may be further dose savings to be made with this system by removing the stationary grid.

Local, multicentre radiation dose benchmarking for coronary angiography and intervention was performed in 2014, demonstrating a median dose of 39.08 $Gycm^2$ for coronary angiography and 87.36 $Gycm^2$ for coronary intervention.(166) This is 29.2 and 65.2 times higher respectively than that of the RFA group in this study with the new system and is 3.6 times and 7.9 times higher than the RFA group with the older system used in this study. However, another study found that DAP for RF ablation procedures were shown to be higher than both coronary angiography and coronary intervention. Although that study did not state whether a lower dose protocol was used for the RF ablation group, or whether the same dose setting and frame rates were used for all procedure groups.(86)

Comparisons have been made to the literature in terms of radiation dose in table 3. Whilst there may be some differences in study methodologies and endpoints between the various studies, the present study demonstrates very low radiation doses across all procedure categories. The results for pulmonary vein isolation (PVI) in this study are comparable to those studies using magnetic guidance systems for AF ablation.(192,193) These systems remove the requirement of fluoroscopy once the initial images are taken. Meticulous dose optimization of fluoroscopy equipment may result in similar radiation dose reduction than that conferred by magnetic guidance systems, which serve primarily to reduce fluoroscopy but also add additional cost. However, magnetic guidance systems have also been shown to reduce procedure duration,(100,105) which is an important factor in a busy institute. Other 3D mapping systems (Carto and NavX) have also been demonstrated to significantly reduce radiation dose and fluoroscopy time.(95) Both these systems were employed for catheter ablation procedures in this study. Studies have also demonstrated that catheter ablation procedures can even be performed without the need for fluoroscopy at all.(96)

The use of magnetic guidance system technologies, in conjunction with optimal imaging equipment and low dose configuration has the potential to reduce radiation doses to very low levels. However, due to its simplicity and ubiquitous availability, fluoroscopy will continue to remain for many EP procedures, particularly if it can be used at the dose levels seen here.

Limitations

This was a retrospective observational study over two years in a single EP laboratory and not a randomised controlled study so there may be confounding factors over the two time periods that were not accounted for. The doses obtained with the older system compare favourably with prior published experience, however, 'fluoro image store' was not available on the old system so comparative fluoroscopy images could not be supplied.

Conclusion

In the EP laboratory, implementation of a contemporary cardiovascular digital imaging system, with meticulous optimization of low dose fluoroscopy settings and continued adherence to good radiation practice principles can result in marked reductions in radiation doses without prolonging procedural time or compromising procedural success. Doses can be reduced to levels comparable to those achieved by magnetic guidance systems, without limiting the use of fluoroscopy.

Conflicts of interest:

None declared.

Current implications

This publication dates back to 2017. The X-ray equipment studied is the latest generation and there are no other publications since that have demonstrated lower doses using a similar strategy. One 2019 publication used a slightly older X-ray system, but still contemporary and investigated dose saving strategies in cardiac device implantations. They used a dose per pulse of 10nGy per pulse as opposed to the 6nGy per pulse in the present study and a pulse rate to 2 PPS, lower than that used in the present study. This resulted in a median dose of 30 CGycm^2 for single chamber devices and 326 CGycm^2 for

CRT devices.(195) By comparison, the doses in the present study are reported as 22 and 410 CGycm^2 , which appear to be similar. A further study in 2019 established a multi-centre DRL for device implants. In that study, median doses obtained were 115 CGycm^2 for single chamber devices and 1410 CGycm^2 for CRT devices. This was not specifically an investigation into low doses but none the less, demonstrates the current situation with median doses across multiple centres.(196)

A further 2019 paper investigated ultra-low dose with a similar X-ray system with a slightly different detector (Siemens Artis Q.Zen). They reported SVT ablation doses of at 429 CGycm2 and 1890 CGycm^2 for AF ablation.(197) This compares to 134 and 710 CGycm2 in the present study which appears to be favourable for the author's institution's continued efforts for radiation reduction and ongoing radiation safety.

Chapter 7 –

J. Crowhurst, M. Savage, V. Subban, A. Incani, O. C. Raffel, K. Poon, D. Murdoch, R. Saireddy, A. Clarke, C. Aroney, N. Bett, D.L. Walters. Factors Contributing to Acute Kidney Injury and the Impact on Mortality in Patients Undergoing Trans-catheter Aortic Valve Replacement. *Heart Lung Circ*. 2016 Mar; 25(3):282-9

Details of my contribution to authorship:

I wrote a research study outline and protocol after reviewing current literature. I designed the study in consultation with local experts (co-authors). I performed a literature review of all relevant, previously published material and reviewed current guidelines. I wrote the research protocol and sought and obtained ethical committee approval. I liaised with relevant experts in the field and obtained permission for use of data from relevant stakeholders. I collected a significant portion of the relevant data.

I analysed the data obtained, performed calculations and statistical analysis. I continued consultation with local experts in the field (co-authors) and as lead author, wrote up the findings before sending out the manuscript for critical review by the co-authors. I liaised with the relevant journals for publication as corresponding author. Peer review required no further changes.

Prologue

Moving on from the risks associated with fluoroscopy and radiation dose, this thesis now investigates the risks of one of the other key requirements for angiography – that being Iodinated contrast media (ICM). ICM is essential for angiography to demonstrate the anatomy and new, contemporary structural heart procedures such as trans-catheter aortic valve replacements (TAVI) require modest volumes of contrast media. Contrast media is known to be toxic to the kidneys(14) and previous studies have shown moderately high rates of acute kidney injury (AKI) following TAVI.(198) This next chapter investigates AKI following TAVI procedures and the relationship with contrast media. It also investigates other predictors of AKI and the impact on hospital stay and mortality.

Factors Contributing to Acute Kidney Injury and the Impact on Mortality in Patients Undergoing Trans-catheter Aortic Valve Replacement

Introduction

Elderly patients with significant aortic stenosis have a poor prognosis without surgery to replace the valve (199). However, they are often deemed too high risk for an operation because of frailty or significant comorbidities (3,199,200). Transcatheter aortic valve replacement (TAVI) is an alternative to conventional open heart surgery in the treatment of severe symptomatic aortic stenosis in this patient group (149,201,202). These patients are at an increased risk of complications, particularly acute kidney injury (AKI). The incidence of AKI in patients undergoing TAVI is reported to be as high as 41.7% (198) and post TAVI renal failure was listed as the most common complication at 30 days in the local SOURCE ANZ registry (203). AKI has been associated with increased length of hospital stay (112,116), 30 day (115) and one year mortality (204).

Iodinated contrast media (ICM) may adversely affect renal function, termed contrast induced nephropathy (CIN) (13). ICM causes cellular injury and death to renal tubular cells (14). In patients undergoing TAVI, the relationship between AKI and ICM is not conclusive, with some studies indicating that ICM use impacts on AKI (205) and others reporting that there is no relationship(115,204,206-210). It is suggested that the high incidence of AKI in this elderly group of patients is multi-factorial, with comorbidities such as age, hypertension (207), peripheral vascular disease (PVD) (198,204) and chronic obstructive pulmonary disease (COPD) (115) being associated with a higher incidence of AKI. To date there are limited local data for AKI incidence and outcomes in patients undergoing TAVI in Australia. This study aimed to investigate AKI in an Australian TAVI centre and investigate how AKI is related to ICM usage, baseline patient characteristics and TAVI procedural data. This study had four aims:

Determine the relationship between ICM volume and AKI in this cohort.

Determine what risk factors or baseline characteristics are related to patients that suffer AKI during TAVI in this cohort.

Determine any procedural factors that have not been previously reported that may predict AKI.

Investigate the impact of AKI on hospital length of stay and early, mid and long term mortality in this cohort.

Material and Method

209 consecutive patients who underwent TAVI procedures between August 2008 and July 2013 were included. The study encompassed TAVI patients in whom either the Corevalve (Medtronic), Edwards Sapien valve (Edwards Lifesciences) or the Lotus Valve (Boston Scientific) were implanted. It excluded those who had a TAVI device implanted in pre existing prosthetic aortic valves and those who had presented for repeat TAVI. It included patients who had TAVI devices implanted from the femoral artery, via the trans-apical approach and via the trans-aortic approach.

All patients were imaged with Iopromide Ultravist 370 mg/cc (Schering AG, Berlin, Germany) contrast media, using a Siemens Artis Zee (Siemens AG, Erlangen, Germany) cardiovascular imaging suite in a hybrid operating theatre. All patients were pre-hydrated with 0.9% sodium chloride saline at a rate of 20 cc/hour unless otherwise indicated.

Baseline patient characteristic data and procedural data were collected prospectively and entered into a database. Other measures were collected post-procedure, including post-procedural complications, blood results, hospital length of stay and mortality at 72 hours, 30 days and 1 year.

AKI was defined in each group by the modified RIFLE classification, as published by the updated Valve Academic Research Consortium definitions (VARC 2) (113). This group defines AKI as an increase in serum creatinine of 150-200% (stage 1), 200-300% (stage 2) or >300% (stage 3). Comparisons were made between patients who did and did not suffer AKI, in terms of baseline patient characteristics, procedural data and outcomes. Approval for this study was granted by the facilities' human research ethics committee.

Statistical Analysis:

Univariate analysis was carried out on all baseline, procedural and follow-up patient characteristics. Categorical variables were compared with a Fisher's exact test and continuous variables with a 2-tailed Students t-test. Multivariate logistic regression was utilised to compare the variables that demonstrated a p-valve >0.1 and that also had >5 events in either group in the univariate analysis. ANOVA calculations were performed to determine significance between AKI stages and mortality. Kaplan Meier curves were created to demonstrate mortality between AKI groups. Significance was determined where probability (P-value) was determined to be < 0.05. SPSS version 20 was utilised for the statistical analysis.

Results

Of the 209 patients in this cohort, 82 developed AKI (39%). Of these 82 patients, 65 had stage 1, 9 had stage 2 and 8 had stage 3 AKI (**figure 7.1**).

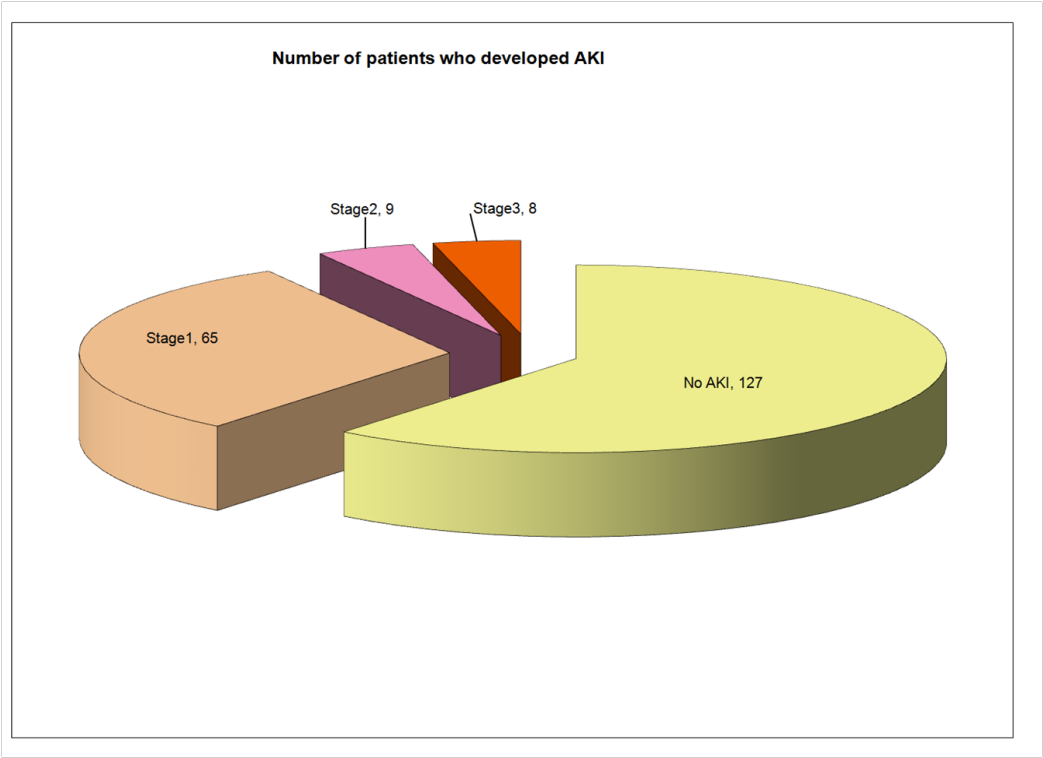

Figure 7. 1 - Numbers of patients who developed AKI.

Legend: Figure 1 demonstrates the number of patients that developed AKI in this study and what severity category they fall into with reference to the criteria laid out by VARC 2 (113). (AKI = Acute kidney injury)

Predictions of AKI from baseline characteristics

Univariate analysis of patient baseline characteristics is demonstrated in **table 7.1**. Of the 27 variables, four reached significance: New York Heart Association (NYHA) class 4, those patients with chronic kidney disease, those with pre-existing anaemia and those with a higher Society of Thoracic Surgeons (STS) (211) score.

Analysis of Blood samples taken

Univariate analysis of the results from blood tests obtained before and after the TAVI procedures indicated that 39% of patients had an increase in their serum creatinine levels consistent with the VARC 2 criteria for AKI (**table 7.2**). This was reflected by a

corresponding fall in their eGFR. Patients who suffered AKI demonstrated lower haemoglobin levels prior to their TAVI procedure and haemoglobin levels were lower in patients who developed AKI post TAVI. Patients with AKI were also more likely to require blood transfusion.

Procedural variables and Mortality

Of the procedural variables (**table 7.3**), AKI was associated with those patients who suffered a procedural stroke (CVA), those that required the valve to be repositioned and those that suffered respiratory failure. Multivariate analysis highlighted CKD and respiratory failure as key predictors of AKI (**table 7.4**).

Table 7. 1 – Baseline Characteristics of patients

Item	Overall	No AKI	AKI	P-value
Number of Patients	209	127 (61%)	82 (39%)	
Age (years)	83.1 (82.2-84.0)	83.6 (82.6-84.7)	82.3 (80.7-83.8)	0.143
BMI	27.5 (26.8-28.3)	27.3 (26.3-28.2)	27.9 (26.8-29.1)	0.384
Male sex (n)	101 (48%)	58 (46%)	43 (52%)	0.395
Previous MI (n)	21 (10%)	11 (9%)	10 (12%)	0.482
Previous CABG (n)	67 (32%)	38 (31%)	29 (34%)	0.650
Previous PCI (n)	67 (32%)	41 (32%)	26 (32%)	1.000
CAD (n)	129 (61%)	79 (62%)	50 (61%)	0.885
Previous PPM (n)	30 (14%)	16 (13%)	14 (17%)	0.425
Diabetes (n)	69 (33%)	37 (29%)	32 (39%)	0.175
Hypertension (n)	162 (78%)	96 (76%)	66 (81%)	0.498
Family History (n)	22 (11%)	14 (11%)	8 (10%)	0.822
Dislipidemia (n)	146 (70%)	88 (69%)	58 (71%)	0.878
Smoking (n)	89 (43%)	52 (41%)	37 (45%)	0.569
Previous Thoracotomy (n)	74 (36%)	41 (33%)	33 (40%)	0.303
NYHA class 4 (n)	6 (3%)	1 (1%)	5 (6%)	0.035
LV Dysfunction (n)	29 (14%)	15 (12%)	14 (17%)	0.310
PAH (n)	48 (23%)	33 (26%)	15 (18%)	0.239
Previous CVA (n)	42 (20%)	20 (16%)	22 (27%)	0.055
PVD (n)	59 (28%)	31 (24%)	28 (34%)	0.157
COPD (n)	84 (40%)	50 (39%)	34 (42%)	0.774
CKD (n)	85 (41%)	35 (28%)	50 (61%)	<0.001
Pre - existing Anaemia (n)	102 (49%)	54 (38%)	48 (59%)	0.033
Previous Cancer (n)	63 (30%)	39 (31%)	24 (29%)	0.878
Previous Radiation (n)	8 (4%)	5 (4%)	3 (4%)	1.000
Logistic Euroscore	19.6 (18.1–21.2)	19.8 (17.7–21.8)	19.4 (17.1–21.8)	0.860
STS Score	5.9 (5.5 – 6.4)	5.4 (5.0 – 5.9)	6.7 (5.7– 7.7)	0.009
STS Score >8	36 (17%)	18 (14%)	18 (22%)	0.189

Footnote: Baseline statistics for the patients involved in this study. All were patients being worked up for re-valving procedures. Median values are given. Numbers in brackets indicate the 95% confidence interval or percentage of the population that exhibits that factor. (AVA = aortic valve area, BMI = body mass index, MI = myocardial infarction, CABG = coronary artery bypass grafts, CAD = Coronary Artery Disease, PPM =

permanent pacemaker COAD = Chronic Obstructive Airways Disease, CVA = Cerebral Vascular Accident, GFR = Glomelular Filtration Rate, LVEF = Left Ventricular Ejection Fraction LVOT = left ventricular Outflow Tract dimension, NYHA = New York Heart Association classification, PVD = Peripheral Vascular Disease. CKD = chronic kidney disease, GORD = gastro-oesophageal reflux disease, CCF = Congestive cardiac failure)

Table 7. 2 - Pre and post-procedure blood sample analysis of patients undergoing TAVI in this study.

Item	Overall	No AKI	AKI	P-value
Number of Patients (n)	209	127	82	
Creatinine Pre µmol/l	101.5 (95 - 108)	90.4 (85 - 95)	119 (105 -131)	<0.001
Creatinine Post µmol/l	140.2 (127 - 153)	98.1 (93 -104)	205 (179 -232)	<0.001
Creatinine Increase µmol/l	38.7 (30 - 48)	8 (5 - 11)	87 (69 - 104)	<0.001
GFR pre	58.9 (56 - 62)	63.9 (61 - 67)	51.1 (47 - 55)	<0.001
GFR post	48.0 (45 - 51)	59.4 (56 - 63)	30.4 (27 - 34)	<0.001
GFR Decrease	10.9 (9 - 13)	4.6 (3 - 6)	20.8 (18 - 23)	<0.001
Haemoglobin Pre (g/L)	124.6 (122-127)	126.1 (123-129)	122.2 (119-126)	0.040
Haemoglobin Post (g/L)	94.8 (93-97)	97.8 (95-100)	90.4 (87-94)	<0.001
Haemoglobin Decrease (g/L)	29.5 (27.5-31.6)	28.4 (25.8-31.0)	31.2 (27.8-34.6)	0.194

Footnote: Blood samples taken before and after TAVI procedure. Numbers in brackets indicate the 95% confidence interval or percentage of the population that exhibits that factor. (GFR = Glomerular filtration rate, CKD = chronic kidney disease, TAVI = Trans catheter aortic valve implant).

Table 7. 3– Procedure based Characteristics of patients undergoing TAVI in this study

Item	Overall	No AKI	AKI	P-value
Number of patients (n)	209	127 (61%)	82 (39%)	
Corevalve (n)	86 (41%)	49 (39%)	37 (45%)	0.389
Edwards Valve (n)	104 (50%)	63 (50%)	41 (50%)	1.000
Lotus Valve (n)	19 (9%)	15 (12%)	4 (5%)	0.138
Surgical Approach (n)	62 (30%)	35 (28%)	27 (3%)	0.440
Multiple Valves Implanted (n)	18 (9%)	8 (6%)	10 (12%)	0.205
Valve Reposition (n)	7 (3%)	1 (1%)	6 (7%)	0.015
Paravalvular AR >2 (n)	5 (2%)	3 (2%)	2 (2%)	1.000
Rapid Burst Pacing (n)	186 (89%)	112 (88%)	74 (90%)	0.821
Procedural Duration (mins)	82.4 (77-87)	81.0 (75-87)	85.2 (77-93)	0.425
Contrast Media Volume (cc)	228 (217-239)	227 (213-240)	231 (212-250)	0.700
Fluoroscopy Time (mins)	19.4 (18.1- 20.7)	19.3 (17.9-20.8)	19.6 (17.2-21.9)	0.875
Liver Dysfunction Post (n)	12 (6%)	0 (0%)	12 (15%)	<0.001
Major Vascular Injury (n)	24 (12%)	15 (12%)	9 (11%)	1.000
Procedural CVA (n)	8 (4%)	1 (1%)	7 (8%)	0.007
Procedural MI (n)	3 (1%)	0 (0%)	3 (4%)	0.059
Respiratory Failure (n)	16 (8%)	4 (3%)	12 (15%)	0.003
Life threatening bleeding (n)	21 (10%)	9 (7%)	12 (15%)	0.099
Transfusion Required (n)	51 (24%)	23 (18%)	28 (34%)	0.013
New Need for Dialysis	5 (2%)	0 (0%)	5 (6%)	0.009
72 Hour Mortality (n)	3 (1%)	2 (2%)	1 (1%)	1.000
30 Day Mortality (n)	11 (5%)	4 (3%)	7 (9%)	0.115
1 Year Mortality (n)	24 (11.5%)	13 (10%)	11 (13%)	0.511
Mean ICU LOS (days)	4.1 (3.3-4.9)	3.2 (2.6-3.9)	5.6 (3.8-7.5)	0.004
Mean Hospital LOS (days)	9.2 (8.2-10.2)	7.5 (6.9-8.2)	11.7 (9.6-13.9)	<0.001

Footnote (Table 7.3): Procedural and post-procedural variables comparing those that suffered AKI and those that didn't. Numbers in brackets indicate the 95% confidence interval or percentage of the population that exhibits that factor. (LBBB = left bundle branch block, ICU = intensive care unit, LOS = length of stay. CVA = Cerebral vascular accident (stroke).

Table 7. 4 – Logistic regression analysis of key variables impacting on AKI

Factor	Odds Ratio	95% CI		p value
		Lower	Upper	
CKD	6.078	1.865	19.808	0.003
Respiratory Failure	27.393	1.953	384.259	0.014
Blood Transfusion	0.202	0.040	1.025	0.054
Previous CVA	4.227	0.831	21.499	0.082
Retrieval Reposition	8.244	0.754	90.106	0.084
Procedural CVA	11.250	0.315	401.415	0.184
NYHA Class 4	5.124	0.374	70.126	0.221
Pre existing Anaemia	1.535	0.438	5.382	0.503

Footnote: This table shows the key variables that demonstrated significance under univariate regression in a multivariate logistic model. It shows that respiratory failure and chronic kidney disease (CKD) are main predictors for AKI. (CVA = cerebral vascular accident, NYHA = New York heart association)**.**

After stepwise removal of non-significant variables, CKD (OR=3.98 (2.14-7.42) p=<0.001), respiratory failure (OR=5.77 (1.68-19.83) p=0.005) previous CVA (OR=2.16 (1.01-4.61) p=0.047) and valve retrieval/ repositioning (OR=11.21 (1.25-100.58) p=0.031) were demonstrated as significant predictors for AKI from the multivariate model. There was an increased length of stay in intensive care for patients with AKI (mean 5.6 days vs 3.3 days p=0.004) and an increased length of overall hospital stay (mean 11.7 vs 7.5 days

p<0.001). There was an insignificant difference in the average volume of ICM used between the AKI and non-AKI groups: 227cc (213-240) vs 231cc (212-250) p=0.700). The difference in average contrast media volume between each of the AKI groups was also insignificant: Stage 0 = 226.8cc (213.3 - 240.2), stage 1 = 234.6cc (212.9 – 256.3), stage 2 = 212.8cc (160.5 – 265.1) and stage 3 = 224.4cc (132.7– 316.1, p=0.864).

Seven patients (4%) were highlighted as requiring the device to be repositioned or retrieved, with six of these developing AKI. Six of the seven were Core valves and one was an Edwards valve via the trans-apical route. None had died within 30 days or one year.

Five patients (2.4%) required dialysis post TAVI. All five had chronic kidney disease (CKD) and had serum creatinine levels over 100 µmol/l prior to TAVI. All five had developed AKI levels 2 or 3. Two had died within 30 days and the remaining three were still alive at one year.

Overall, three patients (1.4%) died within 72 hours of their TAVI procedure, with one of these having AKI. Eleven patients (5.3%) had died at 30 days, with seven of these developing AKI. Twenty four patients (11.5%) had died at 12 months, with 11 of these suffering AKI. Mortality did not reach significance at 72 hours, 30 days or at 12 months between those patients that suffered AKI and those that did not. However, mortality increased with AKI severity. Four of the 127 (3%) that had no AKI, two of the 65 (3%) patients that suffered stage 1 AKI, two of the nine (22%) patients that suffered stage 2 AKI and 3 of the 8 (37.5%) of patients that suffered stage 3 AKI had died at 30 days (p<0.001). No more patients with stages two or three AKI had died at one year than at 30 days post TAVI. The mortality for the different stages of AKI is demonstrated through Kaplan-Meier curves in **figure 7.2**.

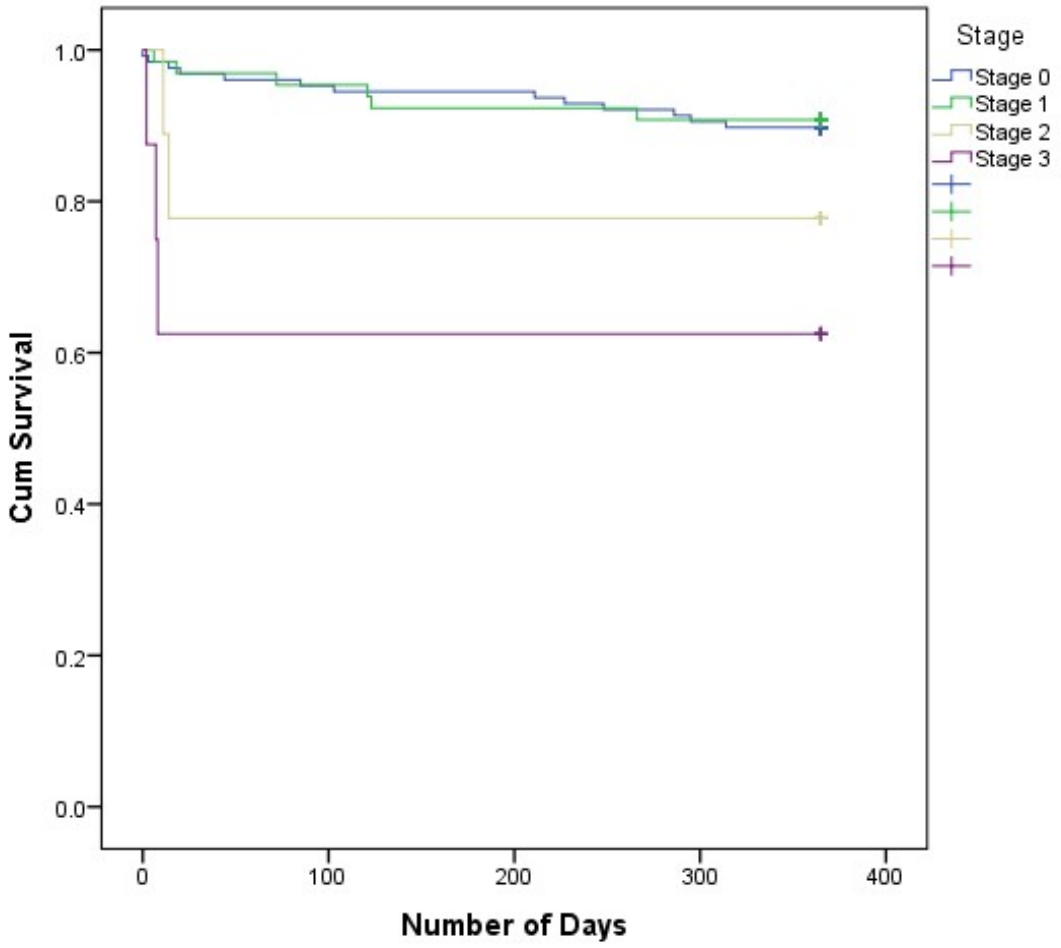

Figure 7. 2 - Kaplan-Meier one year survival for different stages of AKI

Legend: The Kaplan Meier curves demonstrates the survival for patients that suffered AKI in this study. Patients with stage 2 and 3 AKI have a 22% and 38% mortality rate in comparison to the 3% mortality of those that suffered either stage 0 or stage 1 AKI.

Discussion

The 39% overall incidence of AKI in this cohort was higher than some of the literature, (206-208) but similar to the 41.7% seen in others (198). This high incidence may be due to AKI being defined in this study with all 3 stages of the VARC 2 criteria included (113). Only 17 (8%) of the 209 patient cohort suffered either stage 2 or 3 AKI and is consistent with the 8.3% occurrence quoted in another study observing AKI stages 2 and 3 (208). The reason for the high overall incidence is unknown, but AKI has traditionally been linked to ICM usage and CIN and the 228 cc mean volume seen in this cohort is higher than some of the literature (90-219cc) (115,116,205). ICM is associated with AKI as it causes intense and

prolonged vasoconstriction and is toxic to the kidney tubules (14). A large study of 16,248 patients who were administered ICM for radiological examinations demonstrated that the risk of death was 5 times higher for patients who developed AKI (212), which is similar to the experience in TAVI cohorts with AKI (115,204). Importantly, the study by Levy et al demonstrated that renal failure increased the risk of developing fatal non-renal complications. Their study suggested that ICM is strongly linked to AKI (212). However, Bagur et al demonstrated that surgical treatment of aortic stenosis carried a higher incidence of AKI in patients with CKD and that ICM volume was not associated with AKI in their TAVI cohort (115). This finding is echoed in other TAVI studies (204,206-210) and it is seen here in this present study where there was also no significant difference in ICM usage between the AKI groups, indicating that the severity of AKI is not associated with ICM.

Both univariate and multivariate analysis highlighted the existence of CKD as the most significant baseline characteristic in predicting AKI. This finding is echoed in a recent publication of a large TAVI cohort multi-centre registry where the severity of CKD was strongly associated with AKI and patient outcomes (213). In this present study, patients with a high SC prior to TAVI were more likely to suffer AKI post TAVI. These patients had a higher ICU time and a longer hospital stay which has implications for funding in patients suffering AKI post TAVI (116). Also, patients that go on to require dialysis are at a much higher risk of developing CKD (214), which may impact on any future procedures or examinations. Of the five that required dialysis in this study, all presented with CKD, perhaps indicating that the requirement for new dialysis in patients with healthy kidneys is rare. The risk of mortality and renal failure post TAVI has previously been demonstrated to be higher in high risk patients (STS score >8%) (215) and although there was a significant difference in STS scores between the two groups in this present study, this did not correspond to a significant difference in numbers of patients with STS scores of >8%.

In the univariate analysis, baseline haemoglobin and pre existing anaemia were also potential predictors of AKI. Other studies have found baseline haemoglobin not to be a significant predictor (207) but many have noted a fall in haemoglobin post-procedure, which may require blood transfusion (112,115,208). Procedural and post-procedural bleeding and the requirement for blood transfusions are seen as predictors of AKI in this study but this did not seem to impact on mortality, even though in other studies it has (210).

In terms of procedural and post-procedural variables, there was no significant difference between the surgical and femoral TAVI implantation methods in terms of AKI, even though the surgical access route for TAVI has previously been associated with a higher incidence of AKI (112,198,206,207). There was also no significant difference between the TAVI prosthesis types with regard to AKI.

Procedural and post-procedural respiratory failure was seen in 16 patients and under multivariate analysis was highlighted as a significant factor in predicting AKI. In patients with COPD, acute respiratory failure has been highlighted as a major cause of death (216). Acute respiratory failure from COPD increases hypoxia and arterial carbon dioxide levels and may reduce renal blood flow, glomerular filtration and neurohormonal activation (115,217). Although not seen here, COPD has been highlighted as a key factor in predicting AKI (115,204) and COPD has also been previously highlighted as a major predictor of late mortality in TAVI (218).

Repositioning or retrieval of the TAVI prosthesis is demonstrated here to be another predictor for AKI. This is the first time that this variable has been demonstrated to contribute to AKI. This presents another important variable that can impact on AKI. The mechanism for AKI through repositioning is unknown but showering of emboli, causing renal ischemia as the device moves is certainly a possibility. It may be influenced by other factors such as prolonged hypotension from more rapid burst pacing and longer overall procedure time.

In this study, AKI as a whole did not lead to a significant increase in mortality, either in the short term or at 1 year. Mortality in this cohort was low: 5.3% at 30 days and 11.5% at 1 year. However, of those patients that suffered AKI, 20.7% developed stage 2 or 3 AKI and their mortality rate was 22% and 37.5% respectively. This is more in line with other studies (115,204), suggesting that AKI impacts on mortality only if the patient suffers stage 2 or 3 AKI. Acute kidney injury has been linked to an increase in mortality in other procedures, including thoracic percutaneous endo-vascular aortic repair (TEVAR) (219), suggesting that it is not be the valve implant per-se but the invasive nature of these endo-vascular procedures and the associated patient comorbidities.

Conclusion

This study demonstrated that AKI is a common complication of TAVI and that the severity of AKI is important in determining mortality. Acute kidney injury does not appear to be

dependent on ICM volume. Pre-existing chronic kidney disease, respiratory failure, previous stroke and blood tranfusion were highlighted as important predictors for AKI. Transcatheter aortic valve implant device repositioning or retrieval was also identified as a new risk factor impacting on AKI.

Limitations

This was an observational study with all the inherent weaknesses that exist with such. The number of patients was not large and therefore the number of patients was relatively small with respect to the investigation of mortality, though the results clearly demonstrate an increased risk of mortality with severity of AKI. Larger, multi-centre studies should be performed to demonstrate whether these findings are relevant in a larger population. In addition, the study was performed on the first 209 patients undertaken when the TAVI procedure was relatively new and the techniques were still being learnt. This would have an impact on contrast media use and patient outcomes.

Current implications

This study was one of the first studies to publish procedural outcomes for patients undergoing TAVI in Australia. Though it concentrated on AKI, the data collection was substantial and this allowed the detailed procedural outcome investigation and multivariate analysis to be performed. A further publication focused the overall patient outcomes in this cohort, demonstrated good outcomes and mortality compared to other international registries.(220) It is worth noting that there is a learning curve associated with the TAVI procedure. One multi-centre study demonstrated that as centres become more experienced with TAVI, there is an improvement with patient outcomes, with decreased death, and major bleeding. In addition, one study found that contrast media volumes decrease with increased procedural volumes, though in that study there was no difference in the requirement for new dialysis and AKI was not reported.(221) A second study found similar findings with trans-aortic TAVI procedures, where contrast media volumes decreased with increased experience but AKI did not change with increased experience (222)

Chapter 8 –

J. Crowhurst, D. Campbell, O. Raffel, M. Whitby, P. Pathramanan, S. Redmond, A. Incani, K. Poon, C. James, C. Aroney, A. Clarke, D. Walters. Using DynaCT for the Assessment of Ilio-Femoral Arterial Calibre, Calcification and Tortuosity Index in Patients Selected For Trans-catheter Aortic Valve Replacement. *Int J Cardiovasc Imaging.* Volume 29, Issue 7 (2013), Page 1537-1545

Details of my contribution to authorship:

I performed a literature review of all relevant, previously published material and reviewed current guidelines. I had input into sections of the research protocol before ethical committee approval was obtained. I led the collection of relevant data.

I analysed the data obtained, performed calculations and statistical analysis with assistance from Dr Jinlin Fu. I continued consultation with local experts in the field (co-authors) and as lead author, wrote up the findings before sending out the manuscript for critical review by the co-authors. I liaised with the relevant journals for publication as corresponding author and made suggested changes in line with peer review.

Prologue

The previous chapter demonstrates the impact of acute kidney injury on the TAVI patient. Every effort should be made to reduce kidney injury in these patients and reducing the volume of iodinated contrast media is important in that regard. Chapter 8 investigates the potential for rotational angiography (DynaCT) to image the ilio-femoral arterial system in much the same way as traditional multi-slice computed tomography (MSCT), but with lower contrast media volumes. It investigates the ability of this imaging modality in comparison to MSCT in this assessment and any advantages and disadvantages that this modality may have.

Using DynaCT for the Assessment of Ilio-Femoral Arterial Calibre, Calcification and Tortuosity Index in Patients Selected For Trans-catheter Aortic Valve Implant

Introduction

Adequate vascular access for the delivery catheter is fundamental to procedural success in femoral approach Trans Catheter Aortic Valve Implant (TAVI). Vascular access complications are likely to be influenced by the femoral delivery sheath size and patient anatomy(3,201). Patient suitability for trans-femoral AVR will depend on ilio-femoral vessel calibre, the degree of tortuosity and the extent of calcification. If the ilio-femoral access is inadequate, a patient may be considered for trans apical or more currently a trans aortic approach.

Femoral and iliac angiography is well established at providing accurate measurements of the arterial lumen, as is multi-slice computed tomography (MSCT). MSCT also has the benefit of assessing tortuosity and calcification. It is therefore recommended that as a minimum, both femoral angiography and MSCT be performed for patients to be considered for TAVI by the femoral route. Magnetic resonance imaging (MRI) can also perform this role well but it still remains difficult to access in many centres due to the limited number of MRI systems being available.

DynaCT (performing a CT scan using the Cath lab C-arm) has already been proven to be of benefit in TAVI procedures when imaging the aortic root for optimization of fluoroscopic implant angles(137). DynaCT of the ilio-femoral region would require a direct arterial injection and it could easily be performed at the coronary angiography phase of the patient's work-up. It could provide 3D images, as well as a full assessment of vessel calibre, calcification and tortuosity. This cannot be achieved with 2D angiography. A patient who has demonstrable inadequacy of the ilio-femoral arteries (in terms of calibre or tortuosity) with Dyna CT may not require MSCT of the abdomen and pelvis at all, with the potential savings in contrast and radiation. However, DynaCT should be effective in providing vessel calibre measurements, assessing tortuosity and calcification and should match MSCT, arguably the gold standard in this area.

The aim of this study was to scrutinise DynaCT in it's assessment of vessel calibre, tortuosity and calcification of the ilio-femoral tree by direct comparison to the existing imaging methods readily available (angiography and MSCT). Contrast and radiation doses

would also be compared. This was to be performed in the clinical setting, in patients selected for TAVI.

Material and Method

15 patients who were to undergo trans-catheter aortic valve implant at the Prince Charles Hospital, Brisbane, Australia in late 2011 were selected for this study. Prior to the procedure, the patients had coronary angiography, ilio-femoral angiography, contrast MSCT of the chest/abdomen/ pelvis and echocardiography performed as part of their routine work-up for their TAVI procedure. In addition to this, the cohort was to undergo a DynaCT of the ilio-femoral arteries at the time of the procedure. The inclusion criteria included suitable renal function with serum creatinine <100µmol/l and suitable body habitus with a BMI of < 30.

Ethics committee approval was sought and granted for this study by the research committee at the Prince Charles Hospital.

Prospective data was collected of the calibre of the vessels from angiography, MSCT and DynaCT. Pre-determined reference points of the left and right common iliac, external iliac and common femoral arteries were used. These points were:

- Common iliac artery point – 30mm distal to the bifurcation of abdominal aorta.
- External iliac artery point– 30 mm proximal to the mid femoral head.
- Common femoral artery point – at the level of the mid femoral head.

Contrast and radiation dose were also documented and were included in the study for comparison.

Image Acquisition parameters:

Angiography

The angiogram was performed using a Siemens Axiom Artis dBc (Siemens Healthcare Erlangen Germany), at 15 frames per second, using a 5Fr pigtail catheter with 10mm markers. 20mls of Ultravist 370mg/ml contrast media was injected at a rate of 15mls per second into the abdominal aorta just prior to the bifurcation of the common iliac arteries. The unsubtracted image was panned to visualise the length of the ilio-femoral arteries.

The number of injections and volume of contrast media required to visulaise the entire ilio-femoral tree was recorded. Measurements were taken at the reference points and documented.

MSCT

All MSCT scans were performed on the same Siemens Somatom Definition 64slice Dual Source CT scanner Scan parameters were 120kVp, 100-200mAs, 0.5 second rotation time and 0.75mm slice thickness and a 0.5mm table increment. Axial images were reconstructed with a slice thickness of 3mm with an increment of 3mm. The chest, abdomen and pelvis were scanned using 150 mls of intravenous injection (100ml of Optiray 350mg/ml and 50ml of Sodium Chloride) at a rate of 4 ml/s.

DynaCT

The DynaCT was performed using a Siemens Artis Zee dTa with a 30cm x 40cm detector. A 6Fr pigtailed catheter was inserted into the abdominal aorta, proximal to the bifurcation into the left and right common iliac arteries. 33mls of Ultravist 370mg/ml contrast media was diluted with 67 mls of 0.9% Sodium chloride and the 100mls was injected at a rate of 12 ml/second. Rotational angiography was performed using the 8 second DynaCT protocol in which a 200^{o} rotation acquires 397 images in 8 seconds.

Image Reconstruction:

In the MSCT and Dyna CT studies, multi planar reconstructions (MPRs) were created on a *Siemens Syngo Leonardo* workstation that gave a true cross-sectional image of the arteries at the 3 reference points. This is demonstrated in **figure 8.1**. Automatic calibration was achieved through the software of the workstation. Measurements were taken at the reference points using the cross sectional planar images created at each reference point. Examples are demonstrated in **figure 8.2**. The measurements were documented by 2 independent blinded observers.

For the angiogram, measurements were taken from the images acquired at the specified reference points. The pigtail catheter with markers was used for calibration.

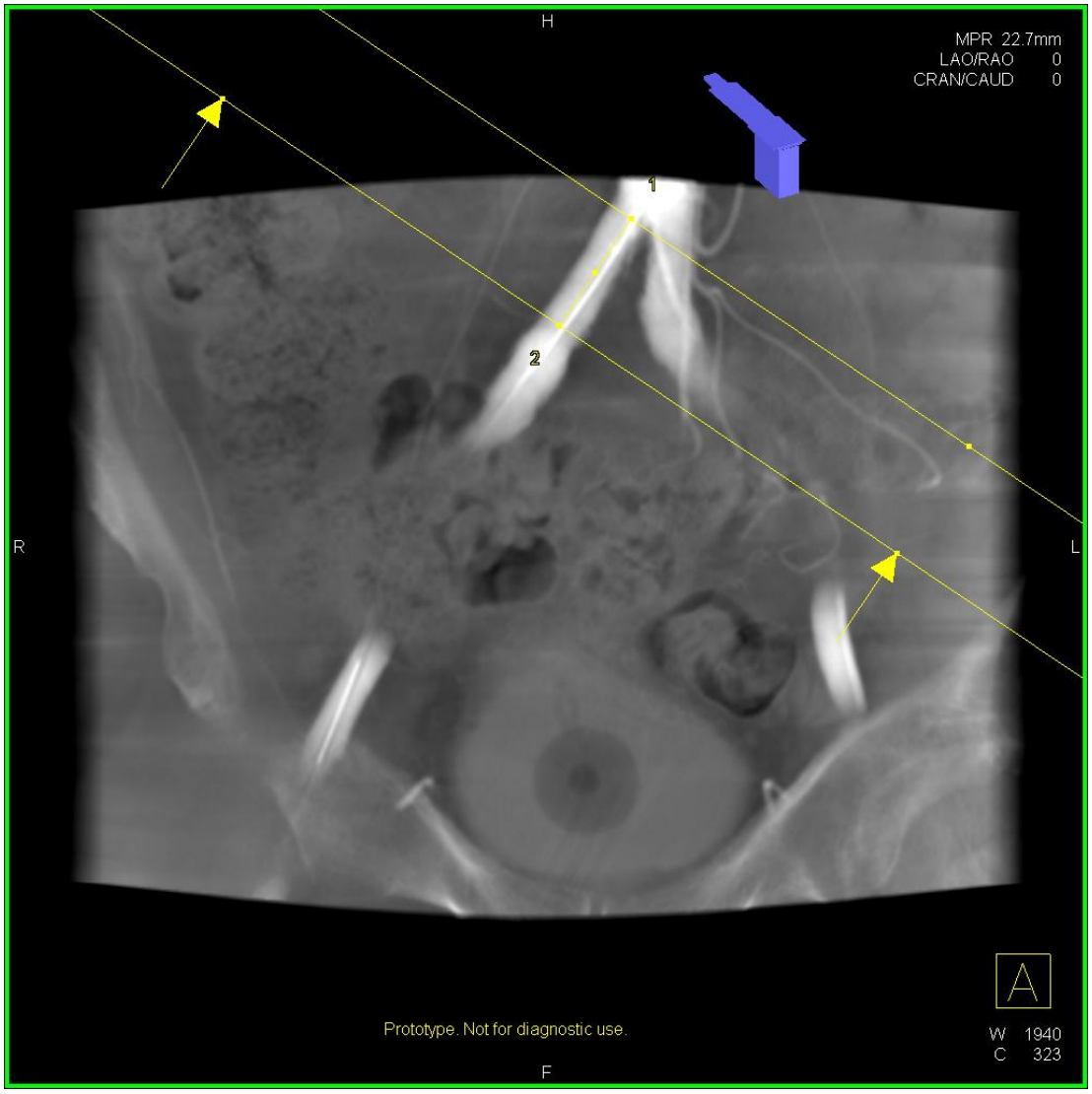

Figure 8. 1 - Screen shot of the MPR creation

Legend:. Image demonstrating production of multi planar, true cross-sectional images of the iliacarteries. In this case, a cross section image is being created 30 mm below the level of the bifurcation (MPR multi-planar reconstruction)

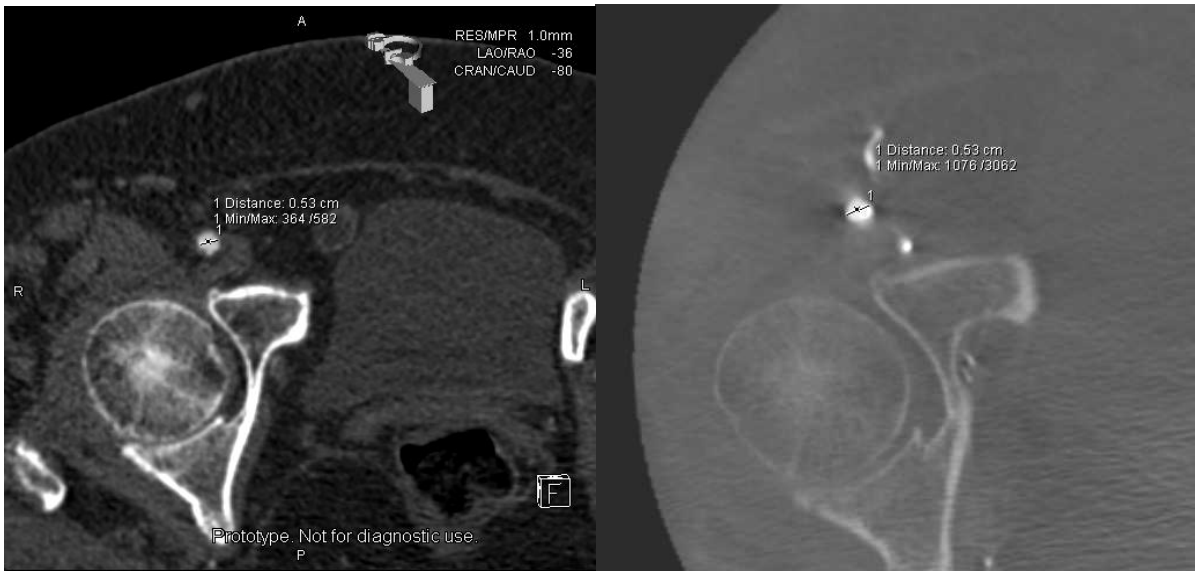

Figure 8. 2 Example images taken of the right femoral artery using MSCT (left) and the respective DynaCT image (right) in the same patient.

Tortuosity:

A novel but simple method of calculating the overall tortuosity of the ilio-femoral artery was developed and utilised in this study. A 3D volume rendered image was created from the MSCT and DynaCT acquisitions using the *Leonardo* workstation and the *Inspace* program (**figure 8.3**). First, the point to point distance was measured from the bifurcation of the iliac arteries to the femoral artery at the level of the mid femoral head. Then the total distance taken by the iliac artery between these points was measured using the *AX vessel analysis tool* on the workstation. This tool gives the length of an artery through its curves and bends. The difference between these two lengths is expressed as a ratio or a 'Tortuosity Index'. This was performed for both the MSCT scan and DynaCT scan. The 2D angiogram was eliminated from this part of the study as the true tortuosity can only be assessed with three planar imaging.

Calcification:

Calcification was scored using a previously established technique(138).The most calcified section of the ilio-femoral tree was recorded on both the DynaCT and MSCT images by two independent, blinded observers and was scored as follows: 0 = no calcification seen, 1 = scanty, 2 = half circumference, 3 = circumferential. For the calcification scores, the mean of the two observers was used to compare MSCT against DynaCT.

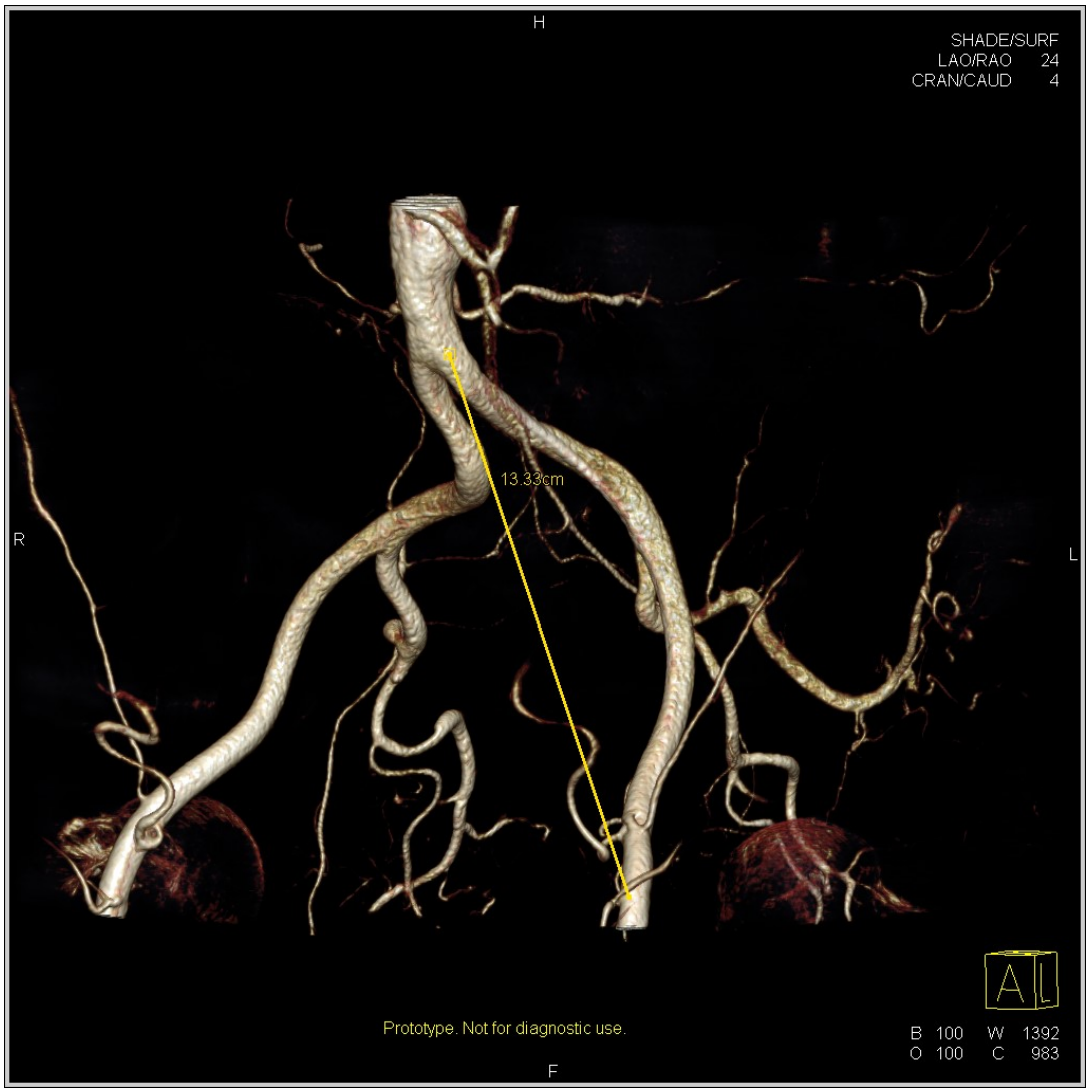

Figure 8. 3 - 3D volume rendered image using DynaCT

Legend: Example of 3D volume rendered Image acquired through DynaCT, demonstrating tortuosity and the difference between the direct distance and the distance taken by the artery. This was used for the tortuosity index calculation.

Radiation Dose Calculations:

Angiography

The effective dose a patient receives for the angiogram section of the study was estimated using PCXMC software (PCXMC Dose Calculations, Version 2.0 Copyright STUK 2008. STUK - Radiation and Nuclear Safety Authority, Helsinki, Finland). This is a Monte Carlo-based dose simulation software. Data collected for this was section the KVp, mAs, radiation dose per pulse, copper filtration, dose area product (DAP), skin entrance surface dose, distance of the patient from the source, distance of the source to the detector and the detector field size.

MSCT

MSCT effective dose was calculated by referring to ICRP 102 (223), using the appropriate conversion coefficients. The conversion coefficients presented in ICRP 102 are with reference to an adult with a standard physique so that the values are estimations only, even though procedure Dose Length Product (DLP) values are exact.

DynaCT

Using the milliamps (mA) and milliseconds (ms) of exposure output by the X-ray system, an effective mAs was determined. This was used in conjunction with the nominal tube output of 40 µGy/mAs which was then corrected for the dose one would receive at 1 m from the source. This value was then scaled to reflect the appropriate field size, then multiplied by the number of total frames, resulting in a DAP that accounted for the mAs of each frame. Once this revised total DAP had been acquired, it was divided into the number of individual projections that that would be considered as part of the simulation as conducted with the use of PCXMC. Once individual effective doses had been calculated for each projection, all effective doses were summed to result in the total effective dose.

Statistical Analysis:

The mean value of the measurements taken at the various anatomical points by the two independent observers for the three imaging methods was used for analysis.

The calibre measurements were compared against one another using concordance correlation coefficients (CCC), and Bland Altman tests. Linear regression was performed for the calibre measurements in the same way as for CCC.

A receiver operator coefficient curve (ROC curve) was used to compare DynaCT against the gold standard, MSCT. In this, a cut-off diameter of 7mm was selected as this was the pre-determined arterial diameter required for access for the 23mm Edwards *Sapien* valve

and is in line with the SOURCE registry criteria (224). A measurement above 7mm was determined as suitable, a measurement below 7mm, determined unsuitable.

The inter-observer variability was compared using correlation coefficients (CC). The tortuosity indices were compared for DynaCT and MSCT using a student t-test**.** Calcification scores between DynaCT and MSCT was assessed using CC. Inter-observer variability for calcification was assessed with a Kappa test. Analysis of the statistical data for these patients was performed using SPSS V16.0.

Results

Patient baseline characteristics and risk scores are outlined in **table 8.1**.

Successful valve implantation was achieved in 14 of the 15 patients, with success being measured as a successful implant without conversion to surgery or death. One of the 15 patients proceeded to a successful aortic valvuloplasty only, without TAVI.

Of the 14 patients that proceeded to TAVI, 5 had Edwards valves implanted and 4 had Corevalves implanted via the femoral approach. The remaining 5 patients had Edwards valves implanted via the trans apical approach.

Mean TAVI procedural fluoroscopy time was 18.7 (± 7.9) minutes. Mean DAP was 23181 (± 9412) $uGym^2$ and mean contrast media volume was 291 (± 72.7) mls.

Vessel Calibre

The mean values of the measurements taken for each anatomical area and how they compare between modalities is given in **table 8.2.** CCC for angiography and MSCT gave a coefficient of 0.96 (95% CI 0.94 to 0.97). In comparison, the CCC comparing angiography to DynaCT was 0.94, (95% CI 0.91 to 0.96). When comparing the two CT methods, DynaCT and MSCT, the CCC was 0.95 with (95% CI 0.92 to 0.97).

Table 8. 1 – Baseline Characteristics of patients

Baseline Characteristics	Value	SD	Median
Age	82.13	6.04	83
Male	5 (33%)		
Height	167.27	14.42	165
Weight	75.33	9.17	79
CAD (n)	10 (66%)		
COAD (n)	4 (27%)		
Sternotomy (n)	6 (40%)		
Previous CVA (n)	3 (20%)		
PVD (n)	6 (60%)		
NYHA	2.8	0.56	3
GFR <60	3 (20%)		
LVEF %	63.33	13.05	68
Aortic stenosis Indicies			
AVA (cm^2)	0.78	0.15	0.75
Mean Gradient (mmHg)	52.82	19.12	50
Peak Gradient (mmHg)	86.81	30.10	85.6
LVOT (mm)	22.2	1.86	22

Footnote: Baseline statistics for the patients involved in this study. All were patients being worked up for re-valving procedures**.** AVA = aortic valve area, CAD = Coronary Artery Disease, COAD = Chronic Obstructive Airways Disease, CVA = Cerebral Vascular Accident, GFR = Glomelular Filtration Rate, LVEF = Left Ventricular Ejection Fraction LVOT = left ventricular Outflow Tract dimension, NYHA = New York Heart Association classification, PVD = Peripheral Vascular Disease.

Table 8. 2 – Difference in measurements across all groups with standard deviation.

Anatomical Area	Angio ±	MSCT ±	Dyna CT ±	P value
Right Common Iliac	9.31 ±1.55	9.53 ±1.72	9.47 ±1.66	0.9309
Left Common Iliac	9.38 ±1.63	9.50 ±1.64	9.19 ±1.84	0.8763
Right External Iliac	7.57 ±1.20	7.60 ±1.22	7.30 ±1.04	0.7385
Left External Iliac	7.65 ±1.17	7.47 ±1.03	7.22 ±0.95	0.5447
Right Common Femoral	7.10 ±1.20	7.26 ±1.10	7.00 ±0.99	0.8040
Left Common femoral	6.92 ±1.05	6.94 ±0.94	6.93 ±0.97	0.9978

Notes: Arterial measurements were taken at predefined points. This table demonstrates the mean value for each imaging modality and the p value obtained across all three methods. MSCT - Multi-slice Computed Tomography

Bland-Altman tests indicate a mean difference (±1.96 standard deviation) between the angiogram and the MSCT of 0.06mm (+0.97, -1.42). The mean difference between the angiogram and DynaCT was 0.13mm, (+1.00, -0.87) and the mean difference between the DynaCT and the MSCT was 0.2mm, (+1.15, -0.76).

Linear regression was performed, where MSCT was determined as the independent variable and DynaCT was determined as the dependent variable, giving $R = 0.96$ ($p<0.001$). When angiography (dependent) was assessed against MSCT (independent), $R = 0.96$ ($p<0.001$). When DynaCT (dependent) was compared to angiography (independent), $R = 0.94$ ($p<0.001$). The Bland Altman and linear regression results are demonstrated graphically in **figure 8.4.**

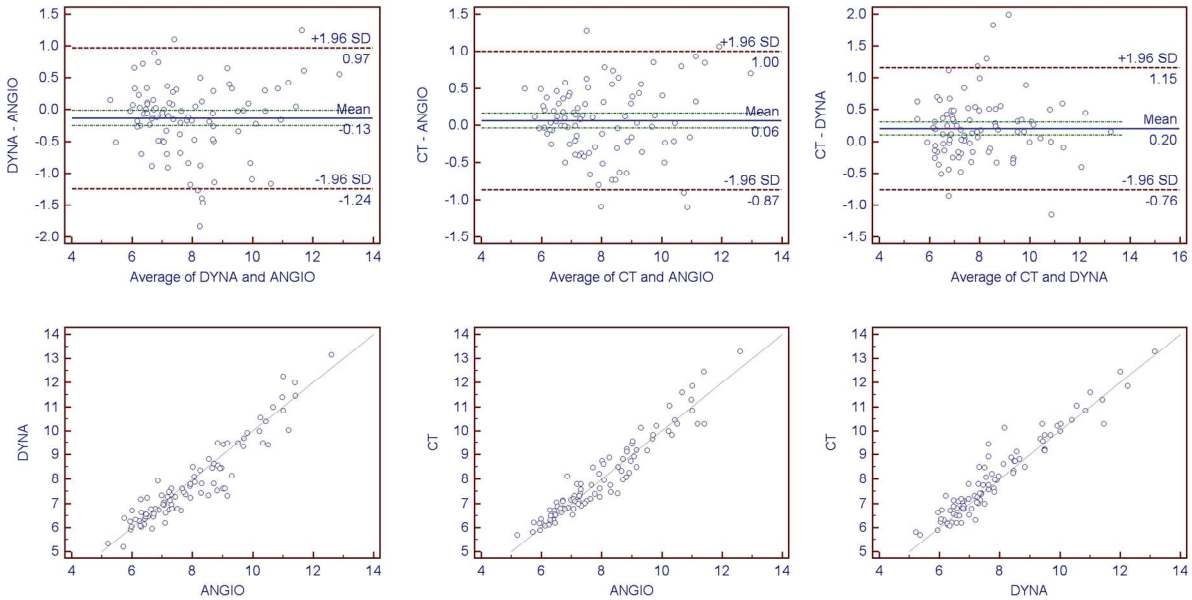

Figure 8. 4 - Bland-Altman and linear regression plots for measurements in mm between Angio, MSCT and DynaCT.

Legend: Bland-Altman plots (top row): where the mean arterial calibre measurements taken with DynaCT are compared to those taken with MSCT and angiography. The small dotted lines demonstrate the mean difference between the modalities compared and the large dotted lines demonstrate 1.95 standard deviations. Linear regression plots (bottom row), demonstrate the arterial calibre measurements for DynaCT in comparison to those taken with MSCT and angiography. (CT = Multi-slice Computed Tomography, Dyna = DynaCT, Angio = Angiography).

The ROC curve demonstrated that with a cut-off of 7mm diameter, 27 of the 90 measurements taken with MSCT were determined unsuitable. When DynaCT was compared against this, 33 of the 90 measurements were deemed unsuitable. The area under the curve was 0.96 (95% CI 0.92 to 0.99) p<0.001. The ROC curve is demonstrated in **figure 8.5**.

When investigating the inter-observer variability for the calibre measurements, correlation was demonstrated between the two operators by Pearson correlation coefficient (CC). The overall CC between the two users was 0.75 (p<0.001). The results were then further split into the separate modalities. Angiography demonstrated a CC of 0.96 (p<0.001) MSCT demonstrated a CC of 0.89 (p<0.001) and Dyna CT, a CC of 0.90 (p<0.001).

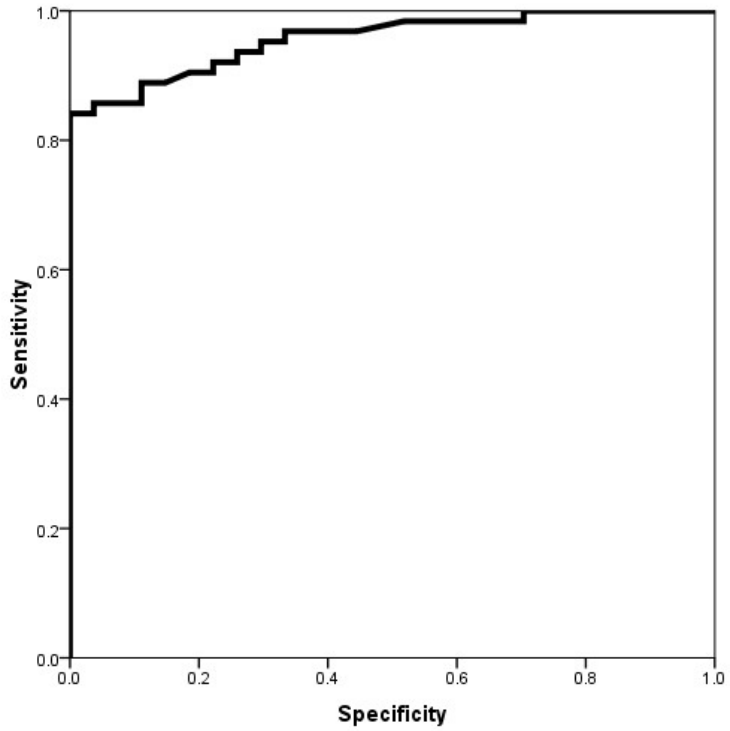

Figure 8. 5 – ROC curve for arterial calibre MSCT and DynaCT

Legend: Receiver Operator Coefficient (ROC) curve for the assessment of vessel calibre using DynaCT when compared against the gold standard: MSCT (MSCT = Multi-slice Computed Tomography).

Tortuosity indicies

The tortuosity of DynaCT and MSCT for both left and right ilio femoral arteries are demonstrated in **Table 7.3**. The results give an overall median tortuosity index of 1.21 (1.19 - 1.25) for DynaCT and 1.31 (1.25 - 1.35) for MSCT (p=0.009). With the catheter in situ, the median tortuosity index was 1.23 (1.17 - 1.26) for DynaCT and 1.33 (1.26 - 1.40) for MSCT (p=0.008). With the catheter absent, the median tortuosity indicies were similar, 1.23 (1.17 - 1.27) for DynaCT and 1.29 (1.03 - 1.31) for MSCT (p=0.472).

Calcification

The average calcification scores of the two observers for DynaCT and MSCT gave a correlation coefficient of 0.245 (p=0.378), **Figure 8.6.**

The calcification scores demonstrated an agreement between the observers of 0.44 ± 0.156 for DynaCT and 0.674 ± 0.179 for MSCT using a Kappa test for inter-observer variability.

Table 8. 3 – Median Tortuosity measurements and Indices summarised - numbers in brackets 95% confidence.

	Dyna CT	MSCT	P value
Overall			
Median Direct Distance	145.35 (138.59 149.25)	146.50 (140.21 151.60)	0.605
Median Arterial Length	174.45 (169.27 179.58)	189.50 (180.83 195.97)	0.003
Tortuosity Index	1.21 (1.19 1.25)	1.31 (1.25 1.35)	0.009
Catheter In situ			
Median Direct Distance	146.75 (135.95 150.36)	146.05 (138.49 153.97)	0.541
Median Arterial Length	172.65 (165.98 180.16)	191.00 (183.5 202.5)	0.001
Tortuosity Index	1.23 (1.17 1.26)	1.33 (1.26 1.40)	0.008
Catheter Absent			
Median Direct Distance	144.85 (139.95 154.26)	146.6 (135.61 155.22)	0.960
Median Arterial Length	177.65 (167.90 185.00)	179.5 (168.28 155.22)	0.489
Tortuosity Index	1.23 (1.17 1.27)	1.29 (1.03 1.31)	0.472

Notes: Median measurements obtained from 3D images using Syngo AX vessel analysis tool. MSCT - Multi-slice Computed Tomography**.**

Radiation and Contrast

Mean effective radiation doses calculated were: 0.57 ± 0.72 mSv (angiography), 7.15 ± 2.58 mSv (MSCT) and 3.63 ± 0.65 mSv (DynaCT).

The median number of acquisitions taken to visualise the ilio-femoral tree using angiography was 2 (95%CI 1.64 - 2.36). The median total contrast volume was 40mls (32.88 - 47.12). This compares to the protocol volumes of 100mls for MSCT and 33mls for DynaCT.

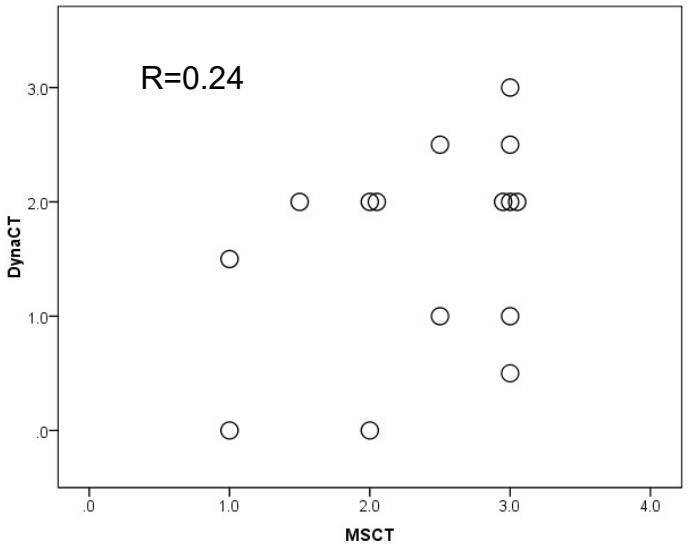

Figure 8. 6 - Correlation of mean calcification scores for MSCT and DynaCT

Legend: Chart demonstrating the correlation of the mean calcification fixed value scores for MSCT and DynaCT. (MSCT = Multi-slice Computed Tomography).

Discussion

In this study, angiography, DynaCT and MSCT values for vessel calibre differ very little using the Bland Altman test, CCC and the linear regression. The strong correlation demonstrates that the measurements of the artery increase at the same rate in any modality and the measurements are accurate in any modality through a range of arterial size.

A femoral arterial calibre of 7mm was desired for implantation of the Edwards Sapien valve in this study, in line with the SOURCE registry criteria (224). The ROC curve analysis demonstrates that when DynaCT is compared to MSCT (the gold standard) for determining arterial calibre, it accurately determined whether an artery was either suitable or unsuitable.

The correlation between the two independent observers for the arterial calibre measurements is strong. These results indicate that the measurements of all modalities are reliably repeatable. This is noteworthy; particularly when one considers that the measurement accuracy is down to 0.1 or 0.2mm. This is confirmed by Norden et al, who also found no gross inter-observer variability in their assessment of DynaCT (138).

The two CT modalities in this study (MSCT and DynaCT) offer the added benefit of assessing the tortuosity in three dimensions as volume rendered images can easily be created. The tortuosity index outlined in this study was developed to give a numerical value to the tortuosity. To our knowledge, this is the first time a numerical value has been given to tortuosity of the ilio-femoral arterial system, though other more complicated systems have been developed for other body areas (225). The results indicate that the catheter within the vessel has an effect on the tortuosity of the vessel due to its stiffness. The tortuosity index calculations indicate that there is no statistical difference between the MSCT and DynaCT in assessing tortuosity with the catheter absent. MSCT is the only modality that demonstrates the vessels in their natural state. This may not be seen as a disadvantage of DynaCT, as the tortuosity of the vessels can be assessed for the practicality of visualising tortuosity with a catheter or sheath in situ. A radial pigtail catheter approach for the DynaCT may be of benefit in future studies as this would demonstrate the femoral arteries in their natural state.

With the calcification scores, the results indicate that there are significant differences between the two modalities in assessing calcification. The calcification was much harder to see with DynaCT than MSCT and this is in line with the study by Nordon et al (138). DynaCT requires more image manipulation (windowing) to visualise the calcium and in many cases was not visible at all. Also, the inter-observer variability was poorly correlated, indicating that the scoring was not easily repeatable. Overall, the results demonstrate that it is not practical to use DynaCT to assess calcification with the methodology used. The contrast/saline ratio may have been too concentrated, causing partial volume artefact, obliterating the delineation of the calcification. Further assessment of DynaCT with lower contrast concentration or without contrast media for calcification assessment may be warranted. The 2D angiogram was not involved in the assessment of calcification because it cannot assess calcification in 3 dimensions and therefore would not fit the methodology used.

The detrimental effect of contrast loading on renal function is well documented (226,227). In our study, the DynaCT was performed with 33 mls, as opposed to a median of 40mls for the angiogram and 100mls for the MSCT. Every effort to reduce contrast loading is important in this patient cohort, in whom the incidence of renal impairment is high. Anything that can reduce contrast load is beneficial (115), particularly if performed immediately prior to surgery (228). A previous study has tried to address this issue with a direct arterial injection during MSCT (134). Our study demonstrates that DynaCT may be

able to perform this role without the requirement of transferring the patient to the CT scanner, sheath in situ.

Radiation dose to the patient is also a consideration in these procedures. The calculated effective radiation dose for the patient using DynaCT from this study is lower than the MSCT but much higher than the angiogram and this agrees with a previous assessment of DynaCT (229). However, it should be noted that the MSCT covers the whole of the aorta and not just the pelvis. It can be used as a screening tool for TAVI patients during their work-up. Other non cardiac related pathology can be detected; with one study demonstrating significant non-cardiac findings in 22.6% of cardiac MSCT scans (230).

A significant difference between the MSCT, DynaCT and angiography is that the latter two are invasive techniques, with the associated risks of arterial puncture (231-233). They also require a direct injection into the abdominal aorta in comparison to the intravenous injection of the MSCT. This is a disadvantage of these modalities, although no complication from arterial puncture was noted in this study.

With DynaCT, the real benefit is its ease of use and the real time processing of the 3D images during the work-up coronary angiogram. It allows a better assessment of the anatomy when compared to 2D angiography in the same setting. On systems with the capability, DynaCT can add useful additional information and may be used instead of 2D ilio-femoral angiography.

Limitations

This is a small study with limited patient numbers. The results for assessing vessel calibre and tortuosity with DynaCT are encouraging. Further studies would be beneficial, particularly with regard to the assessment of calcification.

Conclusion

In patients selected for TAVI, DynaCT correlates very well to MSCT and angiography in the assessment of ilio-femoral arterial calibre. Like MSCT, it can produce 3D volume rendered images, providing valuable information on arterial tortuosity. However, in this study, DynaCT was deemed to be inadequate in the assessment of arterial calcification and inferior to MSCT in this regard.

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Conflict of interest Statement

The Prince Charles Hospital is involved in a research collaboration with Siemens Healthcare. Dr Darren Walters is a consultant for Siemens, Medtronic Inc, a Proctor for Edwards Lifesciences and principal investigator for SOURCE ANZ registry.

There are no other stock ownership, or other equity interests or patent-licensing arrangements within the article.

Current Implications

Rotational angiography or DynaCT is relatively easy to use. The study did, however, demonstrate that the identification of calcification was a weakness of the technology. This is in line with another study investigating the use of DynaCT in assessing the aorta. That study demonstrated that the calcification was not identified as readily and that DynaCT consistently undersized the aortic neck.(138) Since publication, MSCT has become the standard method of anatomical assessment for TAVI as it can image the aortic valve in addition to the femoral arteries in the same examination. In addition, ECG gating is used to avoid artefact of the valve and MSCT can also assess other alternate access routes at the same time. The MSCT is particularly important in assessing vessel size and the degree of calcification.(234) For this reason, there has been no further development of DynaCT in this setting.

Chapter 9 –

J. Crowhurst, K. Poon, D. Murdoch, A. Incani, O.C. Raffel, A. Liddicoat, D. Walters. The Effect of X-ray Beam Distortion on the Edwards Sapien XT™ Trans-catheter Aortic Valve Replacement Prosthesis. *J Med. Radiat. Sci.*; 2015 Dec; 62(4) 239-245

Details of my contribution to authorship:

I performed a literature review of all relevant, previously published material and reviewed current guidelines. I designed the study protocol in consultation with relevant experts in the field (co-authors).

I performed the imaging tests, collected the data and analysed the data obtained. I performed calculations and statistical analysis. I continued consultation with local experts in the field (co-authors) and as lead author, wrote up the findings before sending out the manuscript for critical review by the co-authors. I liaised with the relevant journal for publication as corresponding author and made suggested changes in line with peer review.

Prologue

The previous chapter investigates a new imaging modality in the assessment of patients for TAVI. In this next chapter, the opposite end of the technology spectrum is investigated with regard to TAVI procedures. Chapter 9 investigates the effect of basic X-ray beam distortion on TAVI devices. X-ray beam distortion is a known phenomenon that impacts on all radiographic imaging, including fluoroscopy and is well understood in plain film radiography of larger body parts. During some of these new and complex fluoroscopy procedures, such as TAVI, X-ray production basics may be forgotten, or not deemed as significant. However, as detailed in Chapter 9, the effect of X-ray beam distortion can be significant and should be taken into consideration during these procedures.

The effect of X-ray beam distortion on the Edwards Sapien XT™ trans-catheter aortic valve replacement prosthesis

Introduction

Patients who present with severe aortic stenosis and who are deemed too high risk for conventional open heart surgery can now be offered aortic valve replacement percutaneously.(3,200) Trans-catheter aortic valve implantation (TAVI) is a relatively new procedure which utilises fluoroscopy to percutaneously implant a new aortic heart valve. This is performed without the requirement of open heart surgery and was first described in 2002.(235) Implantation of the Edwards Sapien (Edwards Lifesciences Irvine, CA, USA) trans-catheter aortic valve requires it to be accurately positioned in relation to the aortic valve annulus.(236) Inaccurate positioning can lead to paravalvular regurgitation post implant or even embolisation of the device into the left ventricular outflow tract or ascending aorta.(237) These complications can lead to conversion to open heart surgery, with the associated negative impact on patient outcome.(238)

When implanting the TAVI device, a coaxial or perpendicular X-ray C-arm angle ensures that the three coronary sinuses are aligned in one plane under fluoroscopy and the depth of valve implantation in relation to the annulus can be accurately assessed (**Figure 9.1**).

Ideal positioning is one-third to one-half of the valve above the mid-level of the aortic annulus.(236) With a coaxial angle, the upper and lower stent struts of the implanted valve appear superimposed on the image post implant (**Figure 9.2**).

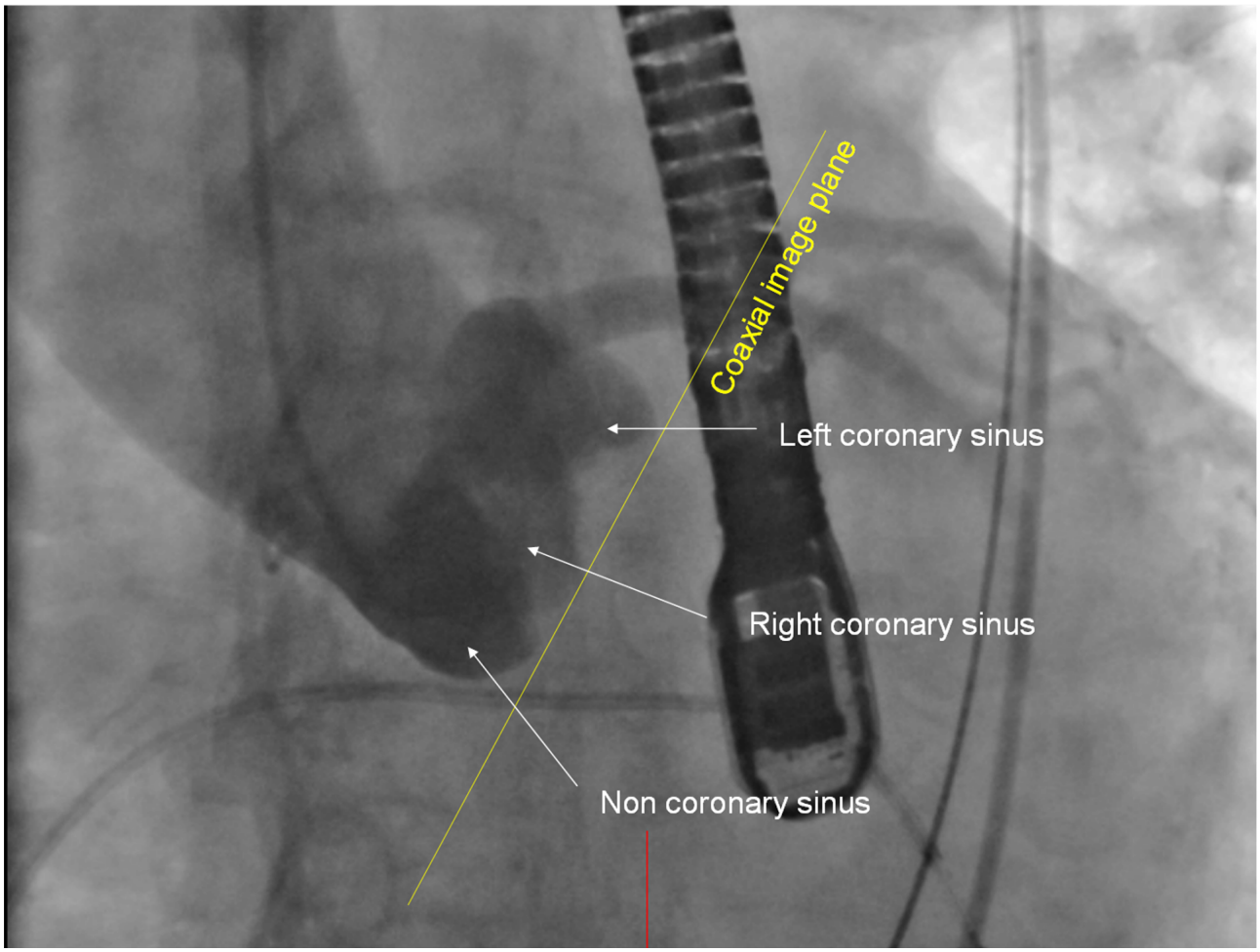

Figure 9. 1 - Pre-implant angiography of the aortic valve.

Legend: This image demonstrates how the three sinuses of the aortic valve are aligned in one plane when the C-arm angle is optimal. The yellow line indicates the coaxial image plane and the level of the aortic annulus, which divides the aorta from the left ventricular outflow tract.

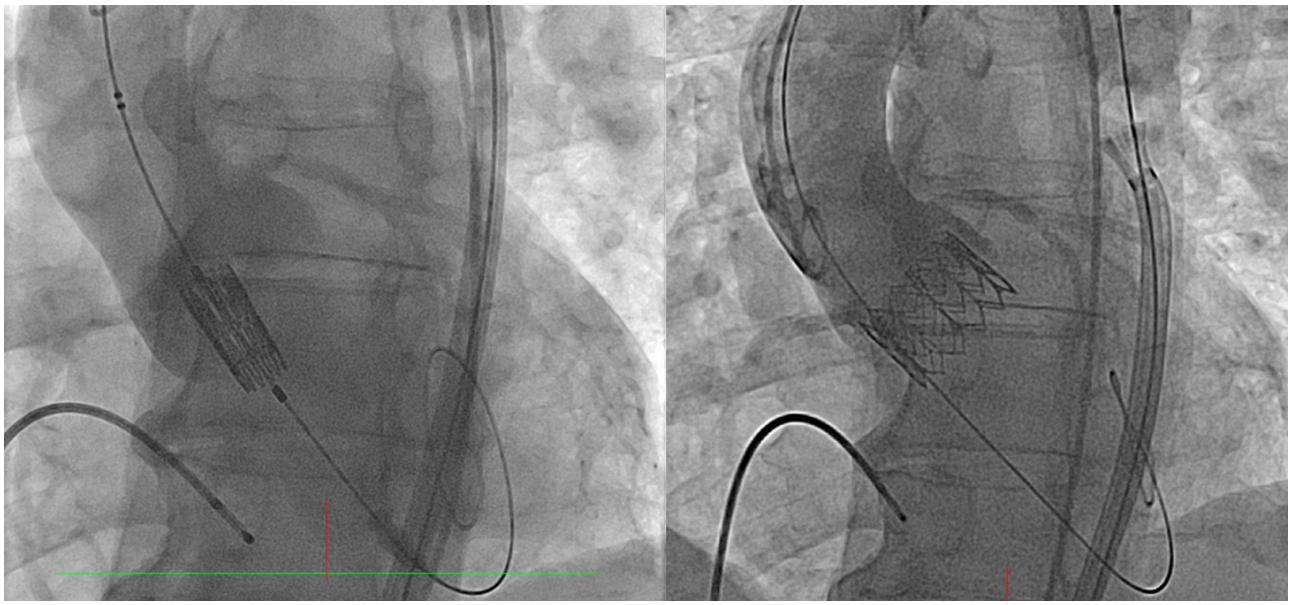

Figure 9. 2 - The trans-catheter aortic valve implant (TAVI) device in the aortic annulus.

Legend: This figure depicts the Edwards Sapien XT^{TM} TAVI device pre- and post-deployment. In this case the appearance of the deployed valve is termed excellent as the anterior and posterior stent struts are almost totally superimposed. It also highlights how good image quality and coaxial valve imaging is important pre deployment to achieve a good prosthesis position.

Previous studies have demonstrated the importance of co-axial imaging. Pre-operative multislice computed tomography (MSCT) or peri-operative cone beam computed tomography (also known as C-arm CT, angiographic CT, and flat-panel CT(135) or 3 dimensional (3D) angiography(136)) can accurately determine the best C-arm angle to achieve coaxial imaging.(136,137,239) Optimising coaxial imaging has also been linked to a decrease in paravalvular regurgitation.(137,240) X-ray equipment vendors have even released specialist software to aid the alignment of the valve sinuses, such is the importance of this phase of the procedure.(137)

The X-ray beam used in cardiovascular imaging systems, is emitted in a cone shaped beam, determined by the small focal spot size and is described as a divergent beam. If an object is not placed in the centre of the image, distortion of the object on the image may occur. This is a well-recognised phenomenon in all radiographic procedures(143) and it is most evident in radiographs using short object film distances and a large field of view (FOV). An example is the antero-posterior projection of the femur, where centring on the

mid femur will mean that the knee joint is exposed to divergent rays and the joint space will appear distorted. In such cases, a second projection would be required to optimally visualise the joint.(241) Distortion is just as relevant during fluoroscopy procedures and in the case of TAVI procedures, which are performed under fluoroscopy, the appearance of the aortic valve could change due to distortion. The valve sinuses may not appear coaxial if the valve is not positioned in the centre of the image, even though the C-arm angle is optimal. This would make the aortic valve appear more oblique and therefore could affect the TAVI device final implant position. The degree of distortion would be demonstrated by a change in the appearance of the TAVI prosthesis' framework post implant. This study aimed to investigate the effect of X-ray beam distortion on the TAVI prosthesis.

Methods

Equipment

Bench-top imaging was carried out on the three currently available *Edwards Sapien* XT™ Valve sizes: 23mm, 26mm and 29mm, using a modern, fluoroscopic system with a flat detector (Siemens Artis Zee, Siemens Healthcare, Erlangen Germany). This X-ray system has annual compliance testing performed by a medical physicist to ensure X-ray beam quality. This is an advanced cardiovascular image system with 3D capability and as such, the manufacturer specifies that the accuracy of C-arm anglulations are to within 0.1 degrees.

Image capture

To investigate distortion, each valve was positioned toward the bottom third of the image field and the C-arm was moved to produce an image where the superior borders of the valve prosthesis frame are superimposed (**Figure 9.3a**). The X-ray table was then moved or 'panned' to position the valve in the upper third of the image field (**Figure 9.3b**). A calibrated sphere measuring exactly 30.00mm was placed in the image field for measurement tool calibration purposes and an image was stored. The C-arm was then rotated with the valve in its new position to once again produce an image where the superior borders of the valve prosthesis frame are superimposed and the number of degrees that the C-arm rotated through to achieve this (as displayed on the X-ray systems data display) was recorded. This was performed to demonstrate the equivalent number of C-arm degrees that the distortion creates.

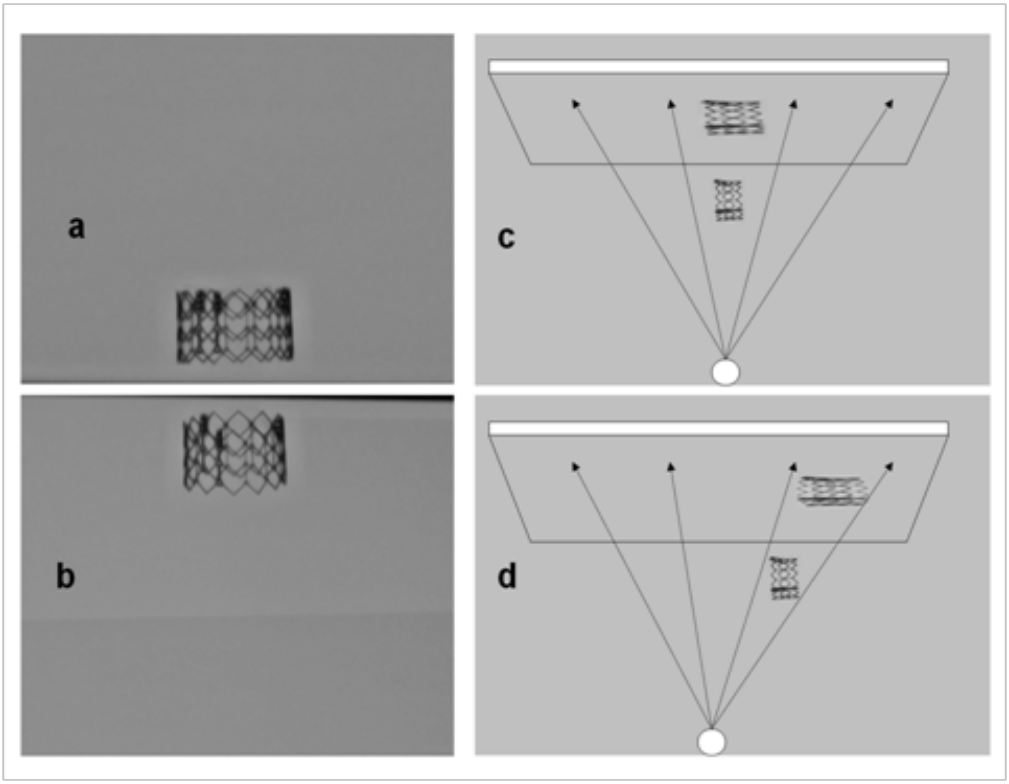

Figure 9. 3 - Change in appearance of the trans-catheter aortic valve implant (TAVI) device as it is moved from the bottom to the top of the image.

Legend: This figure demonstrates how the TAVI device can change in appearance as it is moved from the bottom of the image to the top. (A and B) In this case, a 29 mm valve in a 32 cm field of view (FOV) and its change from excellent in (A) to satisfactory in (B). (C and D) Describes how the TAVI device changes its appearance on the image due to the divergent nature of the X-ray beam and the resultant distortion.

Effect of magnification

In an effort to establish whether any change in appearance was affected by magnification, the above methodology was repeated with the X-ray table height lowered by three 10cm increments from the isocentre (0cm, -10cm and -20cm) and also with the image detector raised in three 10cm increments to change the source to image distance (SID) from 100cm to 110cm and then to 120cm. The above methodology was performed at both a 22cm FOV and a 32cm FOV.

Image analysis

Using a previously published three tier classification tool, one can classify the success of the implant angle, using visual clues from the frame and struts of the newly implanted

valve. *Excellent* refers to perfectly aligned superior struts, where the anterior strut is up to half the height of a cell different to the posterior struts. *Satisfactory* refers to where the superior struts are from half the height of a cell to a whole cell different. *Poor* refers to where the superior struts are more than a whole cell different.(239) These criteria were used to assess any change in the valve appearance due to distortion. Examples of the appearance in the clinical setting are demonstrated in **Figure 9.4.**

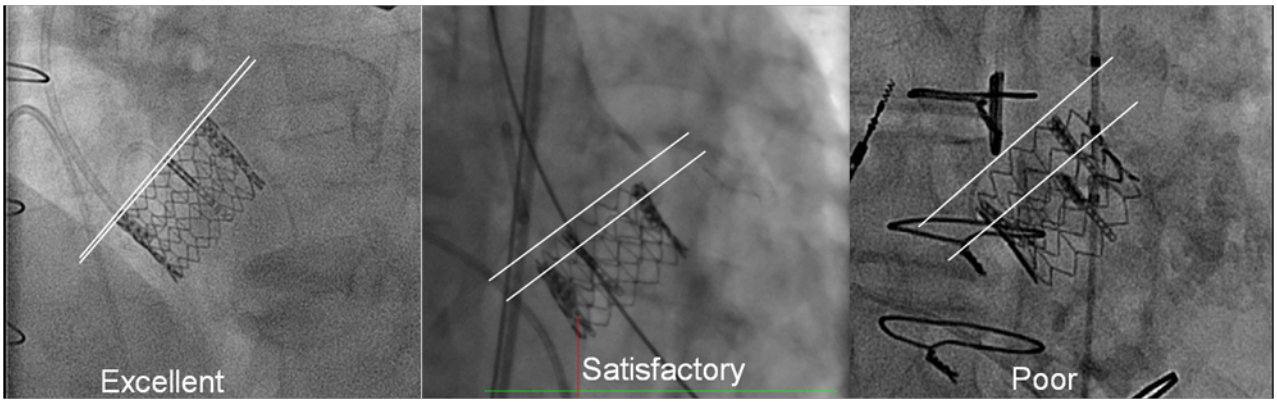

Figure 9. 4 - Clinical examples of the valves appearance using the 3 tier classification tool.

Legend: This figure demonstrates examples of the appearance of the Edwards Sapien valve against the three criteria used in this and other studies. The white lines mark the anterior and posterior upper borders of the valve prosthesis.

The change in appearance and the distance between the superior struts was assessed independently by two cardiac radiographers, with 7 and 19 years of experience respectively. These observers used the X-ray systems measurement tool to numerically quantify any change in appearance. Calibration of the measurement tool was performed against the 30.00mm sphere. Correlation of the observers measurements were assessed using a Pearson's correlation coefficient. This study was a bench-top study and did not involve human subjects. Human research ethics approval was therefore not required.

Results

Overall, the distortion was not sufficient to change the appearance from excellent to satisfactory on any valve size at any magnification when using a 22cm FOV. However, when a 32cm FOV was used, the distortion was sufficient to change the appearance from excellent to satisfactory in certain conditions. The detail of the results of the benchtop testing is shown in **Tables 9.1 and 9.2**. The two observers scored the valves appearance against the 3 tier classification tool with 92.3% agreement. The Pearson's correlation coefficient showed good agreement between the observers for the numerical measurement of the distorted prosthesis appearance: $R=0.96$, $P<0.001$.

Table 9. 1 – The results of benchtop testing with the Edwards Sapien XT valve imaged in a 32cm field of view and the effect of distortion.

Valve Size (mm)	FOV (cm)	SID (cm)	Table Height (cm)	Distance Table is moved to position valve from bottom to top of image (cm)	Appearance score	Mean Distance between superior stent struts as measured on the image (mm)	Equivalent C-arm Angulation (degrees)
29	32	100	0	16	Satisfactory	5.1	10
		100	-10	14	Satisfactory	5.4	10
		100	-20	11	Satisfactory	4.7	8
		110	0	14	Satisfactory	4.3	10
		110	-10	12	Satisfactory	4.4	9
		110	-20	10	Satisfactory	4.5	7
		120	0	14	Satisfactory	4.0	8
		120	-10	12	Satisfactory	4.4	9
		120	-20	9	Sat/Ex	3.4	6
26	32	100	0	15	Satisfactory	4.9	11
		100	-10	14	Satisfactory	5.1	10
		100	-20	11	Satisfactory	4.9	8
		110	0	13	Sat/Ex	4.1	9
		110	-10	11	Excellent	4.4	9
		110	-20	10	Excellent	4.2	8
		120	0	12	Sat/Ex	4.2	9
		120	-10	10	Excellent	4.3	8
		120	-20	9	Excellent	4.1	7
23	32	100	0	16	Satisfactory	4.1	10
		100	-10	14	Satisfactory	4.0	10
		100	-20	12	Satisfactory	3.8	9
		110	0	15	Sat/Ex	3.5	10
		110	-10	14	Excellent	4.0	10
		110	-20	11	Excellent	3.9	8
		120	0	14	Excellent	3.2	10
		120	-10	12	Excellent	3.3	9
		120	-20	10	Excellent	3.2	8

Footnote: The table demonstrates how each of the 3 Edwards Sapien valves changes its appearance due to the image distortion created by the divergent beam in a 32cm field of

view. The distance between the anterior and posterior struts is quantified and the angulation required to bring the valve back to a coaxial angle is demonstrated. Disagreement in appearance score between the observers is demonstrated by a combined score (e.g. Sat/Ex). (FOV = field of view, SID = source to image distance)

Table 9. 2 – The results of benchtop testing with the Edwards Sapien XT valve imaged in a 22cm field of view and the effect of distortion.

Valve Size (mm)	FOV (cm)	SID (cm)	Table Height (cm)	Distance Table is moved to position valve from bottom to top of image (cm)	Appearance score	Mean distance between superior stent struts as measured on the image (mm)	Equivalent C-arm Angulation (degrees)
29	22	100	0	10	Excellent	3.7	7
		100	-10	9	Excellent	3.0	6
		100	-20	7	Excellent	3.1	5
		110	0	9	Excellent	2.4	4
		110	-10	8	Excellent	2.4	5
		110	-20	7	Excellent	2.5	6
		120	0	8	Excellent	2.3	4
		120	-10	7	Excellent	2.2	5
		120	-20	6	Excellent	2.8	5
26	22	100	0	9	Excellent	2.8	6
		100	-10	8	Excellent	2.5	6
		100	-20	6	Excellent	2.5	4
		110	0	9	Excellent	2.4	7
		110	-10	8	Excellent	2.4	5
		110	-20	6	Excellent	2.5	5
		120	0	7	Excellent	2.0	6
		120	-10	7	Excellent	2.2	5
		120	-20	6	Excellent	1.7	3
23	22	100	0	12	Excellent	2.7	8
		100	-10	10	Excellent	2.5	7
		100	-20	9	Excellent	2.3	6
		110	0	10	Excellent	2.4	7
		110	-10	8	Excellent	2.4	7
		110	-20	8	Excellent	2.3	7
		120	0	9	Excellent	2.5	7
		120	-10	7	Excellent	2.2	6
		120	-20	7	Excellent	2.2	5

Footnote: The table demonstrates how each of the 3 Edwards Sapien valves changes its appearance due to the image distortion created by the divergent beam in a 22cm field of

view. The distance between the anterior and posterior struts is quantified and the angulation required to bring the valve back to a coaxial angle is demonstrated.

(FOV = field of view, SID = source to image distance)

Discussion

The effect of distortion from beam divergence is well understood in radiography and the principles are described in radiographic imaging technique text books.(143,241) Specific tools have even been designed to cater for the change in appearance of lateral lumbar spine radiographs due to distortion.(242) However, the effect of beam distortion has not been discussed before in relation to TAVI procedures. The effect may be most relevant during transaortic TAVI procedures, where the TAVI device is inserted through the superior aspect of the ascending aorta. During these procedures, visualisation of the insertion sheath under fluoroscopy is required to ensure that it is perpendicular to the valves annular plane.(243) This scenario has the most potential to position the valve away from the centre of the image.

In this study, the greatest distortion of the valve is seen when the FOV is large (32cm) and the magnification is low (detector low and table high). With this combination, the table can be moved further whilst still being able to visualize the valve in the image. This places the valve further from the photons that are travelling perpendicularly between the X-ray tube and detector, increasing the distorted appearance. With this scenario, the appearance of the valve changes to the equivalent to rotating the C-arm by up to 11 degrees. The cut off for the valve changing from *excellent* to *satisfactory* appears to be between 10 and 6 degrees of equivalent C-arm rotation, depending on the FOV used and the valve size.

The results also indicate that magnification does not greatly affect the degree of distortion visualized until the larger FOV is used. With this in mind, the 22cm FOV is normally used for the set-up aortogram and subsequent valve deployment. This configuration also electronically magnifies the image to better visualize the detail of the anatomy and prosthesis. However, it is noted from the results that under high geometric magnification, only small table movements or only a few degrees of C-arm angulation will distort the valve's appearance This is problematic in clinical practice where a small deviation from the optimal C-arm angle or table position has a large effect on the appearance of the valve. Therefore geometric magnification should be avoided or minimized. This issue may be highlighted again during procedures with trans aortic access, where there may be a

tendency to increase the height of the detector away from the patient to enable better access and visualization of the access site by the surgeon. This will increase magnification. The valve size is also shown here to influence the degree of distortion, with the 29mm valve distorting more than the 23mm, under the same beam geometry. This is due to the fact that with the larger valve, the distance between the upper and lower stent struts is greater and are therefore projected further apart onto the detector.

The appearance of implanted TAVI devices against the 3 tier classification tool used here was investigated in detail in the clinical setting in 2013. That study demonstrated that by using cone beam CT and specialist software to predict the best C-arm angle, an excellent appearance could be achieved in 84% of cases, compared to 42% without. It demonstrated that more aortograms and fluoroscopy were required to obtain the desired coaxial appearance in the group where cone beam CT was not used. The main finding in that study however, was that with an e*xcellent* appearance, paravalvular regurgitation (leakage around the valve) from non-optimal TAVI device position was significantly lower.(137) This is clinically important as even mild paravalvular regurgitation has been associated with increased mortality at 2 years post procedure.(113,149) In another study, low positioning of the TAVI device has also been associated with a greater incidence of ECG rhythm disturbances, again highlighting the importance of accurate positioning.(244)

The results in this study demonstrate that, as expected, moving the TAVI device from the bottom to the top of the image distorts its appearance. The clinical application of these findings is that the set-up angiogram, with a co-axial valve sinus appearance and the subsequent deployment of the valve must be performed with the valve positioned in the centre of the fluoroscopic image. Maintaining the native valve in the centre of the image as the prosthesis is positioned is of the utmost importance. Performing the initial aortogram with the valve positioned in one part of the image and deploying the valve in another could lead to inaccurate positioning from distortion. The team performing TAVI procedures should be aware of the existence of beam distortion and its potential to impact on final valve positioning. Practical ways to avoid prosthesis malposition from distortion are summarized in **Table 9.3.**

Table 9. 3 – Practical ways to avoid valve prosthesis malposition from distortion.

Practical ways to avoid valve prosthesis malposition from distortion
Ensure that the initial aortogram is performed with the native valve in the centre of the image. Use pre-operative CT or peri procedural cone beam CT to predict the coaxial C-arm angle for better accuracy. Use a small field of view. Avoid excessive geometric magnification as small changes in C-arm/table movements will have a greater effect on distortion. Ensure that the valve prosthesis is deployed in the centre of the image.

Limitations

This study was a bench-top study with a theoretical conclusion that the distorted appearance could lead to device mal positioning. Future studies could investigate the effect of distortion and its impact on deployment position of TAVI devices into 3D aortic models. Also, while this study concentrated on the Edwards valve prosthesis, it is likely that the other prosthesis types would demonstrate similar results.

Conclusion

Much effort is spent achieving coaxial imaging to ensure accurate TAVI position in relation to the aortic valve annulus. However the basic radiographic effect of fluoroscopic beam distortion has the potential to affect coaxial imaging and the final TAVI device position.

Current Implications

Since publication, there have been no further studies in the literature on the effect of beam distortion in TAVR from the C-arm as described here. This chapter remains a unique body of work and still remains relevant.

Chapter 10 - Discussion and Conclusions

There is consistent growth in the number of cardiac angiography procedures performed each year(152) and the treatment options using percutaneous interventions continues to increase. This thesis contributes significantly to the evidence based practice model of advanced cardiac angiography.

This thesis has covered the three main topics of angiography that would be relevant to the radiographer working in cardiac catheterisation laboratories. These items are: radiation dose and dose reduction to patients and staff, the impact of contrast media on kidney function and the assessment of imaging technology in new and developing types of procedures. This thesis pulls together these elements into a cohesive package and would be very relevant reading for radiographers and cardiologists undertaking contemporary and emerging procedures in cardiac catheterisation laboratories.

Firstly, radiation dose in cardiac catheterisation laboratories was investigated. When investigating radiation dose, it is important to measure dose for the procedures performed and compare them to established benchmarks. However, the benchmarks that exist in the literature are from other countries. This may have implications as the workflow, regulations and licensing may be different from those in Queensland and Australia and this may impact on the reference level. Therefore, before investigating radiation dose at an individual facility, it is important to establish a local benchmark. As the international committee for radiation protection (ICRP) point out; diagnostic reference levels (DRLs) and benchmark levels for patients should be compared to national benchmarks.(7) As a result, the first part of this thesis was to establish a multicentre reference level for coronary angiography and intervention, given the paucity of data surrounding reference levels for radiation dose to patients undergoing cardiac angiography. **Chapter 2** of this thesis demonstrated Australia's first large scale multi-centre reference level study for both diagnostic and percutaneous coronary intervention procedures in Queensland public hospitals, something that has not been achieved to date in Australia. The levels observed are consistent with those published in the literature, as evidenced in **tables 2.3 and 2.4** of this thesis.

Once the reference levels are established, it is then a natural progression to investigate the factors that may impact on patient radiation dose. When considering the reference level, one should investigate locally the factors that would lead to doses above the DRL(7)

which is usually established as the third quartile value.(15,22,245) This has been encompassed within **chapter 3.** However, in addition to investigating patient dose, this study also investigates high radiation doses (>75th percentile) to the doctors (operators) performing these procedures. The operators stand close to the patient and as such are subjected to radiation that scatters backwards from the patient. Given some of the high profile publications of the effects of radiation on operators,(62-64) it is important to investigate this. The study outlined in **chapter 3** is the largest study to date investigating high radiation doses to operators, with over 2500 observations. Again, the higher doses (>75th percentile) were investigated and using multivariate analysis, it was possible to demonstrate that in addition to biplane imaging and male patients, patient obesity was the factor with the highest predictive value to lead to a high dose in both patients and operators, after correcting for all other variables. Other studies in the literature on this topic are mostly of a small sample size and many only investigate the impact of changing one variable that impacts on radiation dose to the operator such as the arterial access route.(47) The authors study in **chapter 3** investigated how embedding the use of the personal dosimeter into everyday practice, worn by each individual operator for each individual procedure, can give valuable detail when matched to a procedural database. The combined radiation exposure and procedural data obtained gives a comprehensive insight as to which procedures and variables within each procedure give the higher doses. This study is the most comprehensive to date on this important topic. It has shown that radiation dose is multi-factorial, and that patient obesity has the highest predictive value of a high radiation dose to both patients and staff.

Once reference levels and the factors that lead to high doses are established, it is then a natural progression to reduce dose, which leads us to **chapter 4**. In **chapter 4** I demonstrate that occupational radiation dose is not just a concern for the primary operator. Other staff members stand close to the patient during cardiac angiography and interventional procedures. Percutaneous intervention for structural pathology of the heart requires a larger team than for angiography, as the patient is often anaesthetised, requiring anaesthetic staff. In addition, adjunctive imaging is also often utilised, such as trans-oesophageal echocardiography (TOE). The TOE imaging operator is a cardiologist at the authors centre, and they stand close to the patient for the majority of the procedure whilst X-rays are being used. As the study in **chapter 4** demonstrated, radiation dose to the TOE operator was the highest of the team, which led to an additional shield being

installed. The dose reduction from the use of the additional shielding demonstrates the dramatic impact that additional shielding can have to TOE operator radiation dose.

Given the high doses and the proven benefits of the shielding, the authors advocate the use of additional shielding like this in all catheter laboratories performing structural intervention requiring TOE guidance. This study is pivotal in radiation protection in the modern era and has the potential to alter radiation safety guidelines worldwide and dictate future catheter laboratory design. This chapter uncovers a previously unreported consequence in the percutaneous treatment of cardiovascular disease and the importance of this work is demonstrated by the Journal of the American College of Cardiology (JACC) accepting this paper for publication. Further, the editors chose this paper to be the continuous medical education (CME) article for the issue. For this, the journal editors invited this author to write a clinical scenario and a series of multiple choice questions that are related to the paper. The readers of the journal could then read the paper, answer the quiz and gain extra CME credits. This additional CME work is outlined in **Appendix v** of this thesis. An editorial was also published in the same issue of JACC, based on the paper in this thesis, written by Hirshfeld et al who congratulated this author and the team on the work.(246)

Continuing the theme of dose reduction, **chapter 5** was an editorial that this author was invited to write on the topic of radiation dose reduction in coronary angiography. The editorial was based on a paper by Badawy et al that reduced dose by lowering the fluoroscopy dose rate in conjunction with modifying the image processing protocol used by the X-ray system.(33) The editorial covered the reasons why radiation dose reduction should be considered and the methods that can be utilised to reduce dose in angiography. The editorial then concentrated on the publication of Badawy et al(33) and compared that study to others in the literature, in addition to expert commentary on the topic. It summarised that sensible reductions in fluoroscopy pulse rates can reduce overall radiation dose significantly and that this can benefit not only the patient but also the staff working in the room.

The concept of dose reduction by reducing the fluoroscopy pulse rate in the Badawy et al(33) study is not a dissimilar methodology to that used in reducing radiation dose during electrophysiology procedures, highlighted in **chapter 6** of this thesis. This paper was published in 2017 and demonstrated that using modern equipment, properly configured for low dose fluoroscopy can result in very low levels of radiation for electrophysiology procedures. Electrophysiology procedures were investigated because they have

previously been associated with high doses.(86) The X-ray system used for electrophysiology procedures at The Prince Charles Hospital was being replaced during the candidature period and was an excellent opportunity to investigate the impact of introducing a new system on radiation dose. The results are remarkable and they demonstrate that contemporary x-ray equipment can have a huge impact on radiation dose for these procedures. In that study, radiation doses to patients were reduced by 90% through the utilisation of modern, readily configurable equipment, when compared to equipment of a previous generation, without a reduction in fluoroscopy time. At the time of submission to the target journal, the doses seen from this low pulse rate, optimally configured system were the lowest published to date in the literature. However, by the time of actual publication, other studies emerged,(110) with slightly lower dose that were included in the authors eventual publication. However, where other studies have demonstrated low doses for only one procedure type,(105,192,247) the authors study is unique, as it that demonstrates extremely low doses can be obtained for all procedures performed in a modern contemporary EP laboratory. The doses seen from this system are extremely low and demonstrate what can be achieved with a contemporary, dose optimised X-ray system.

We have seen from the work in **chapter 4** that as contemporary complex structural procedures, such as TAVI gain momentum, one must be mindful of the risks to the patient and staff. These new procedures bring their own challenges, such as occupational radiation. However, radiation is not the only risk from angiography, iodinated contrast media (ICM) and the resulting acute kidney injury (AKI) are also significant problems for the patient. AKI is linked to ICM volume(14) and currently, this is particularly important because the patients undergoing the TAVI procedure are elderly and have multiple co-morbidities. **Chapter 7** investigates this problem and whether contrast media volume is linked to the incidence of AKI and whether patients suffering AKI post TAVI have a poorer outcome. The paper in **Chapter 7** demonstrates that AKI severity is not necessarily due to an increased ICM volume administered but is due more to pre-existing co-morbidities such as chronic kidney disease and procedural factors such as device repositioning. In addition, it found that patients have a poorer outcome in terms of length of hospital stay and 30 day mortality in this study. These findings are consistent with others in the literature,(208) as were the predicting factors for AKI, such as chronic kidney disease(207) and the need for blood transfusions.(112) However, one new determining factor for AKI that was discovered

was that of device repositioning or retrieval. This was the first time that this procedural complication had been associated with AKI and is of great importance moving forward. The paper in this chapter was published using the initial data from an Australian TAVI program. As such, the procedural contrast media volume was higher than some others in the literature. It is worth noting that there is a learning curve associated with the TAVI procedure. One multi-centre study demonstrated that as centres become more experienced with TAVI, there is an improvement with patient outcomes, with decreased death, and major bleeding. In addition, contrast media volumes decrease with increased volumes, though in that study there was no difference in the requirement for new dialysis and AKI was not reported.(221) A second study found similar findings with trans-aortic TAVI procedures, where contrast media volumes decreased with increased experience but AKI did not change with increased experience.(222)

TAVI is a relatively new procedure and it requires critical imaging assessment of both the valve anatomy and the arterial access.(248) Building on previous work in assessing c-arm CT (DynaCT) for imaging the aortic route for TAVI procedures,(137) advances in X-ray system c-arm capabilities in the assessment of the ilio-femoral arteries have been explored in **chapter 8** of this thesis. The authors hypothesised that DynaCT could produce similar images of the ilio-femoral anatomy to MSCT by using the angiography c-arm and using much less ICM volume than MSCT. This could mean that patients may not have to have their ilio-femoral arteries imaged at all with MSCT, reducing the ICM load at the work-up stage. The study in **chapter 8** demonstrated that the fluoroscopy c-arm can create images similar to a conventional MSCT scan of the same area and that measurements of the anatomy are of a similar level of accuracy to 2D fluoroscopy and MSCT. In this study a new and novel method for calculating the tortuosity of the ilio-femoral arteries is described. This method was simple; it created a ratio of the distance taken by the artery between the femoral head and the aorto-iliac bifurcation compared to the direct distance. This was called the *tortuosity index*. The study did, however, demonstrate that the identification of calcification was a weakness of the technology, which is in line with previous studies.(138) It is therefore perceived that MSCT will remain the mainstay of pre-operative assessment for TAVI into the future. This technology demonstrates great potential and as computing power, image manipulation and artificial intelligence evolve, a greater utility of this and other similar techniques will undoubtedly emerge.

The final publication of this thesis demonstrates that even though we are in a new contemporary era of percutaneous treatments, such as TAVI, these intervention devices can still be prone to basic X-ray beam distortion from the divergent nature of the beam. X-ray beam distortion is well understood by radiographers and it is well described in undergraduate radiography text books.(143) As demonstrated in the paper Poon et al,(137) where implant angles were shown to impact on paravalvular leak, much effort is taken to implant the device in the optimal c-arm angle, so as to position the device correctly in the aortic annulus. The bench-top study in **chapter 9** demonstrates that TAVI devices can appear oblique if implanted near the periphery of the image, even though the angle of the c-arm may be ideal. This study demonstrates that it is extremely important to always position the aortic root in the centre of the image when performing angiography and also to always deploy the TAVI device in the centre of the beam. This is very important for optimal valve positioning and may help prevent paravalvular regurgitation, which affects patient outcomes.

Ionising radiation will undoubtedly be used for years to come for diagnostic and interventional cardiac procedures. This thesis has investigated the areas of radiation dose, acute kidney injury and imaging techniques in a new era of increasing complexity and an ever-increasing range of options for percutaneous cardiac treatment under X-ray guidance. The use of angiography in cardiovascular disease continues to evolve and this thesis has highlighted some of the problems associated with this technology and some ways to combat those problems as we move forwards.

- Future Directions

The study published in **chapter 2** of this thesis was published in 2014. (166) One of the recommendations of that paper was that the diagnostic reference level (DRL) calculation should be repeated every five years. This is particularly relevant as technologically superior X-ray systems are developed and brought into clinical use. As technology improves, radiation doses from X-ray systems may lower the DRL. However, procedures are becoming more complex and lengthy and DRLs for different and new procedures should be created. The DRL study should be re-visited for cardiac angiography within Queensland public hospitals in the very near future. Additionally, it should be extended to include other procedures that are performed in high volumes at most centres, such as permanent pacemaker implants.

Reduction in radiation dose outputs from X-ray systems will also affect the radiation doses to the staff in the room. There is a great need to continue to monitor radiation doses to staff to ensure that their doses reduce as time goes on. Additionally, interventional cardiologists should have benchmarked doses for procedures. These staff should know what radiation dose they will be exposed to for the procedures that they perform. If doses are monitored on a cases by case basis, for a sufficient period of time, we can build a picture of what doses cardiologists are being exposed to for a range of procedures. In effect, a DRL can then be created for operator dose. This would be readily achievable using the methodology outlined in **chapter 3**.

In a similar manner to the methodology to that outlined in **chapter 4**,(171) other staff in the room should also be monitored. The assistant to the primary operator should have their doses evaluated on a case by case basis, as their doses have not been published to date, and may be different to that of the primary operator, with different influencing factors. This is a body of work that should be undertaken to better understand their doses and factors that may influence high doses and this is readily achievable.

The results of **chapter 7**(249) demonstrated that contrast media volume did not appear to be associated with acute kidney injury in patients undergoing TAVI. This is an interesting topic and further work is required in trailing prophylactic methods to reduce the incidence of AKI in patients with pre-existing renal impairment. Further, the fact that contrast media volume has not been associated with AKI in numerous studies(112,115,249) suggests that a deeper understanding and further studies on contrast induced nephropathy in TAVI patients is required.

C-arm CT continues to evolve performing for procedures requiring computed tomography (CT) examinations peri-operatively. It is apparent, however, that there may need to be further developments in X-ray detector technology to improve the ability of c-arm CT systems to image vessel calcification. In addition, MSCT and has firmly positioned itself as an essential pre-requisite for anatomical assessment prior to TAVI procedures.

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Appendices:

Appendix i: Awards and accolades relating to this work.

- 2013 - Certificate of appreciation – Metro North Hospital and Health Services - Allied Health - Collaborative Cross discipline Research Activities
- 2014- Australian Institute of Radiography Research Scholarship - $10,000 - Competitive research grant.
- 2015- Best abstract award - Nurses and Technicians EuroPCR 2015.

  Establishing radiation dose levels during TAVI procedures for the patient and the multidisciplinary heart team.
- 2016 – Nominated - Metro North Hospitals CAHRLI Allied Health Research and Innovation Award.
- 2016 – Nominated - Metro North Hospitals Research Excellence Award as part of TAVI program.
- 2016 – Appointed as a Visiting Fellow QUT Clinical sciences faculty – Clinical supervisor for Honours students
- 2016 – Finalist - Metro North HHS Staff Excellence Award – Leadership Category – Awarded *Highly commended*. For number of papers and abstracts in five years.
- 2018 – Nominated - Metro North Hospitals Research Excellence award – Complex Healthcare Challenges category. *Reducing radiation exposure to echocardiographers.*
- 2018 – Highly commended - Metro North Hospitals staff excellence award – Innovation *Reducing radiation exposure to echocardiographers.*
- 2018 – Winner - Prince Charles Hospital staff excellence award – Innovation *Reducing radiation exposure to echocardiographers*
- 2018 – Nominated – Queensland Health staff excellence award – Innovation *Reducing radiation exposure to echocardiographers*
- 2019 – Winner – Graeme Neilsen Award – TPCH Best published paper of 2018

  Radiation Exposure of Operators Performing Transoesophageal Echocardiography during Percutaneous Structural Cardiac Interventions.

Appendix ii: Best abstract award - Nurses and Technicians EuroPCR 2015.


CALL FOR NURSES & TECHNICIANS ABSTRACTS

James Crowhurst

has been awarded this certificate for best Nurses and technicians presentation at EuroPCR 2015

Friday 22nd May, 2015

On behalf of the Board of Directors,

Alberto Cremonesi
EuroPCR Course Director

Jean Fajadet
EuroPCR Course Director
EAPCI Past President

William Wijns
EuroPCR Course Director
Chairman of PCR

Stephan Windecker
EuroPCR Course Director
EAPCI President

Appendix iii: Ethics approval letters

Enquiries to: R&ETPCH@health.qld.gov.au
Office Ph: Anne_Carle@health.qld.gov.au
(07) 3139 4198
Our Ref: (07) 3139 4500
AC/JL/Exemption

Queensland Government

16 December 2013

Human Research Ethics Committee
Metro North Hospital and Health Service
The Prince Charles Hospital
Administration Building, Lower Ground
Rode Road, Chermside QLD 4032

Mr James Crowhurst
CIU The Prince Charles Hospital
Chermside 4032

Dear Dr Crowhurst

Re: HREC/13/QPCH/337: Radiation Dose In Coronary Angiography and Intervention: Initial Results From the Establishment of a Multi Centre Diagnostic Reference Level In Queensland Public Hospitals

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Committee reviewed the above project submitted on 12 December 2013.

I wish to acknowledge that the proposal does not require full HREC review on the basis of the project is a clinical audit/ quality activity. This exemption is subject to the following conditions:

- If the project has not commenced within 3 months, please advise the Coordinator, HREC.
- The project must be carried out in accordance with the National Statement on Ethical Conduct in Human Research 2007.
- Please provide an annual report on the outcomes of this project.
- If the results of your project are to be published, please include an appropriate acknowledgement of the relevant department/s who have supported this project.
- The HREC may audit the conduct of any project reviewed under NHMRC guidelines. This may include consultation with the Principal Investigator and/or a visit to the research site by members of the HREC.

Office	Postal	Phone
Research, Ethics & Governance Office	Administration Building, Lower Ground	(07) 3139 4500
The Prince Charles Hospital	Rode Road, Chermside Q 4032	(07) 3139 4198

- Please advise the Human Research Ethics Committee of the date you intend to commence the project.

On behalf of the Human Research Ethics Committee, I would like to wish you every success with your project.

Yours sincerely

Anne Carle
Executive Officer
Research, Ethics and Governance Unit

Enquiries to: R&ETPCH@health.qld.gov.au
Office Ph: Anne.Carle@health.qld.gov.au
(07) 3139 4198
Our Ref: (07) 3139 4500
AC/JI/Exemption

Queensland Government

15 December 2014

Human Research Ethics Committee
Metro North Hospital and Health Service
The Prince Charles Hospital
Building 14
Rode Road, Chermside QLD 4032

Jim Crowhurst
Radiographer Investigations Unit
The Prince Charles Hospital

Dear Dr Crowhurst

Re: HREC/14/QPCH/275: Factors Impacting on Patient and Operator Radiation Dose During Percutaneous Cardiac Intervention

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Committee reviewed the above project submitted on 11 December 2014.

This is to confirm that this project meets the National Statement definition of a project that is exempt from full ethical review on the basis that this is an audit/quality assurance project.

The documents reviewed and approved for the above mentioned project include:

- Project Summary dated 10 December 2014.

This exemption is subject to the following conditions:

- If the project has not commenced within 3 months, please advise the Coordinator, HREC.
- The project must be carried out in accordance with the National Statement on Ethical Conduct in Human Research 2007.
- Please provide an annual report on the outcomes of this project.
- If the results of your project are to be published, please include an appropriate acknowledgement of the relevant department/s who have supported this project.

- The HREC may audit the conduct of any project reviewed under NHMRC guidelines. This may include consultation with the Principal Investigator and/or a visit to the site/s by members of the HREC or their delegate.

- Please advise the Human Research Ethics Committee of the date you intend to commence the project.
(http://www.health.qld.gov.au/tpch/documents/form_notification.dot)

On behalf of the Human Research Ethics Committee, I would like to wish you every success with your project.

Yours sincerely

Anne Carle
Executive Officer
Research, Ethics and Governance Unit

Enquiries to: R&ETPCH@health.qld.gov.au
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Our Ref: (07) 3139 4500
AC/JL/Exemption

Queensland Government

6 November 2015

Human Research Ethics Committee
Metro North Hospital and Health Service
The Prince Charles Hospital
Building 14
Rode Road, Chermside QLD 4032

Dr Jim Crowhurst
Cardiac Investigations Unit
The Prince Charles Hospital

Dear Dr Crwohurst

Re: HREC/15/QPCH/276: Radiation Dose Reduction Electrophysiology Procedures Using New Generation x-ray Technology and an Optimised Equipment Configuration

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Office reviewed the above project submitted on 16 October 2015.

This is to confirm that this project meets the National Statement definition of a project that is exempt from full ethical review on the basis that this is an audit/quality assurance project and it complies with the NHMRC guidance document *"Ethical Considerations in Quality Assurance and Evaluation Activities"* 2014.

The documents reviewed and approved for the above mentioned project include:

- Proposal dated 15 October 2015

This exemption is subject to the following conditions:

- If the project has not commenced within 3 months, please advise the Coordinator, HREC.
- Notify the TPCH HREC office if there are any changes to the project which may affect this opinion.
- If the results of your project are to be published, please include an appropriate acknowledgement of the relevant department/s who have

supported this project.

- The HREC may audit the conduct of any project reviewed under NHMRC guidelines. This may include consultation with the Principal Investigator and/or a visit to the site/s by members of the HREC or their delegate.

On behalf of the Human Research Ethics Committee, I would like to wish you every success with your project.

Yours sincerely

Dr Russell Denman
Chair
The Prince Charles Hospital Human Research Ethics Committee

Enquiries to: RGOTPCH@health.qld.gov.au
Office Ph: (07) 3139 4198
(07) 3139 4407
Our Ref: Governance Approval

Queensland Government

11 June 2014

Research Governance Office
Metro North Hospital and Health Service
The Prince Charles Hospital
Administration Building, Lower Ground
Rode Road, Chermside QLD 4032

Mr Jim Crowhurst
Cardiac Investigations Unit
The Prince Charles Hospital

Dear Mr Crowhurst

SSA14/QPCH/105
HREC/13/QPCH/308: Procedural outcomes and impacts on mortality - The Prince Charles Hospital TAVI program

Thank you for submitting an application for authorisation of this project. I am pleased to inform you that authorisation has been granted for this study to take place at the following site:

THE PRINCE CHARLES HOSPITAL

The following conditions apply to this research proposal. These are additional to those conditions imposed by the Human Research Ethics Committee that granted ethical approval.

1. Proposed amendments to the research protocol or conduct of the research which may affect the ethical acceptability of the project are to be submitted to the HREC for review. A copy of the HREC approval/rejection letter must be submitted to the RGO;
2. Proposed amendments to the research protocol or conduct of the research which only affects the ongoing site acceptability of the project, are to be submitted to the research governance officer;
3. Proposed amendments to the research protocol or conduct of the research which may affect both the going ethical acceptability of the project and the site acceptability of the project are to be submitted firstly to the HREC for review and then to the research governance officer after a HREC decision is made.

I am pleased to advise Governance approval of this research project. The documents reviewed and approved include:

Document	***Version***	***Date***
Site Specific Application (AU/11/8B07118)	1	26 February 2014

Please complete the Notification of Commencement Form once commencement of this protocol has occurred at this site (http://www.health.qld.gov.au/tpch/documents/form_notification.dot) and return to the office of the Human Research Ethics Committee.

On behalf of the Research, Ethics and Governance Unit, we wish you every success in your research project.

Yours sincerely

Anne Carle
CEO Delegate
Metro North Hospital and Health Service

(1)

Queensland Government

A/Prof Darren Walters
Cardiology Clinical Research Centre
5th Floor, Clinical Sciences Building
The Prince Charles Hospital

Queensland Health
Human Research Ethics Committee
The Prince Charles Hospital
Metro North Health Service District
Rode Road,
Chermside QLD 4032
Executive Officer (07) 3139 4500
Research & Ethics Ph:
Office Ph: (07) 3139 4691
Fax:: (07) 3139 6907
Our Ref: PL/JL/ Low Risk Approval

7.18

FILE COPY

5 May 2011

Dear A/Prof Walters,

Re: HREC/11/QPCH/26: Pilot study on the use of syngo Aortic ValveGuide prototype software in the selection of patients for transcatheter aortic valve implantation. D. Walters

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Committee reviewed your submission and upon recommendation, the Chair has granted final approval for your low risk project.

Approval of this project is subject to the same confidentiality and privacy requirements as apply to other research projects and research subjects are not recognisable in publications or oral presentations.

Please complete the Commencement Form before starting your study and return to the office of the Human Research Ethics Committee. http://www.health.qld.gov.au/northside/documents/form_notification.dot

If you intend to publish the results of your work, it is advisable to ascertain from prospective journal editor/s the actual requirements for publication e.g. some journals may require full ethical review of all studies. When results are published, appropriate acknowledgment of the hospital should be included in the article. Please forward copies of all publications resulting from the study for inclusion in the Internet website list.

On behalf of the Human Research Ethics Committee, I would like to wish you every success with your research endeavour.

Yours truly,

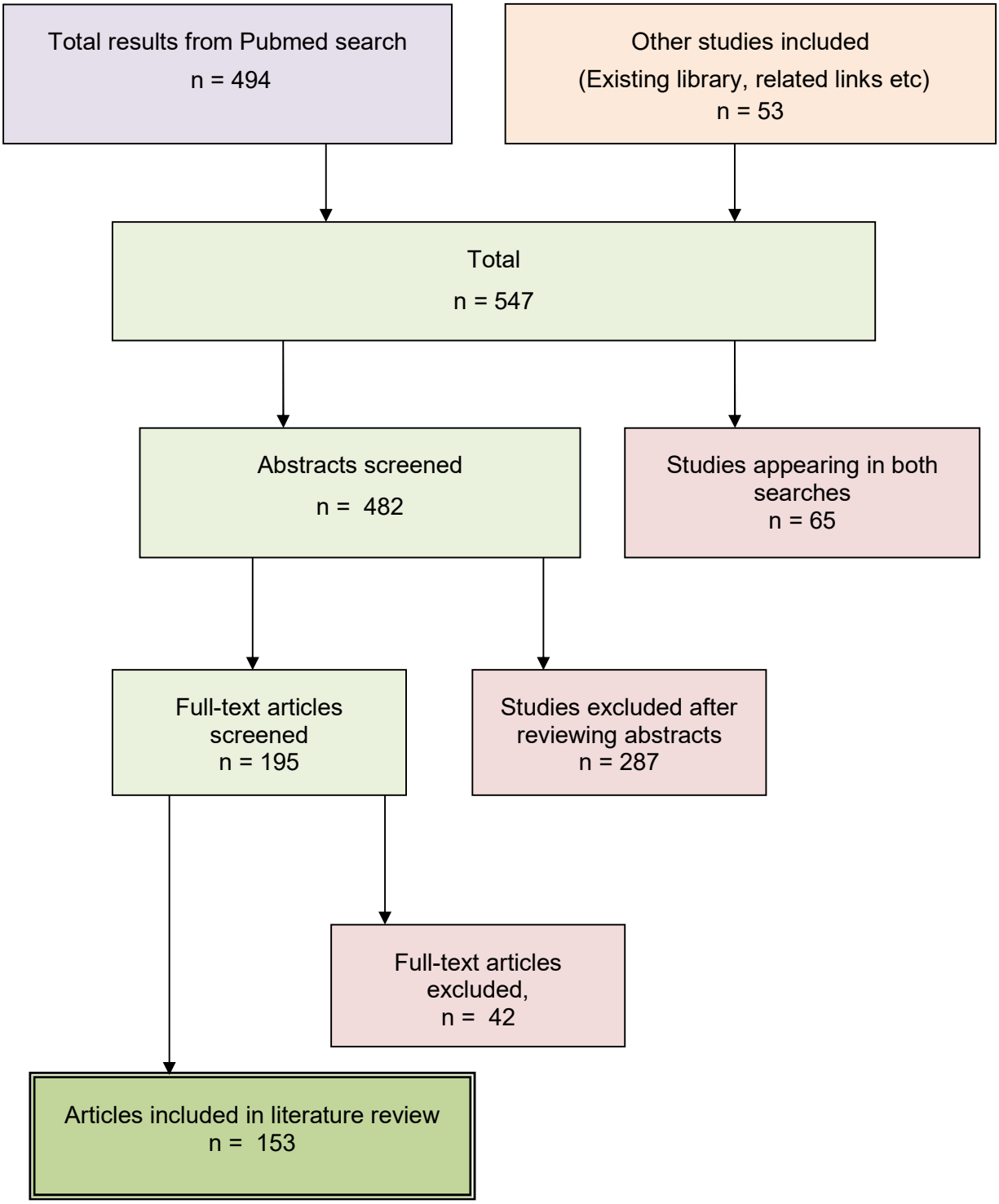
Dr Russell Denman
Chair
HUMAN RESEARCH ETHICS COMMITTEE
METRO NORTH HEALTH SERVICE DISTRICT

Appendix iv: Literature review searches.

Search Terms in Pubmed:

- Radiation dose and cardiac angiography and patient AND "last 10 years"[PDat] Not computed not CT
- Radiation dose and cardiac angiography and operator AND "last 10 years"[PDat]
- Radiation dose AND electrophysiology
- Dyna CT) AND transcatheter aortic valve replacement)
- ((computed tomography) AND femoral artery) AND transcatheter aortic valve replacement
- ((rotational angiography) AND transcatheter aortic valve replacement)
- ((acute kidney injury) AND transcatheter aortic valve replacement) AND contrast media
- (((contrast media) AND transcatheter aortic valve replacement) NOT computed tomography) NOT CT
- ((parallax) AND radiology) NOT computed tomography
- ((divergent beam) AND radiology) NOT computed tomography

Literature review methodology flow diagram



Appendix v: Continuous Medical Education – JACC

In 2018 I was invited to write a continuous medical education (CME) supplement for the Journal of the American College of Cardiology based on the paper outlined in chapter 5 of this thesis that was accepted to their journal. The work completed is outlined below:

American College of Cardiology Foundation
JACC Journal CME Activity Selection worksheet

For each CME activity, please email a copy to Eileen Cavanagh: ecavanagh@acc.org

Today's Date: ___2/12/18_____

1. Journal: JACC
2. Article Title: Radiation Exposure of Operators Performing Transesophageal Echocardiography during Percutaneous Structural Cardiac Interventions
3. Running Title: Radiation Dose to TEE Operators
4. Issue: March 20, 2018
5. Abstract: Background: Transesophageal echocardiagraphy (TEE) operators provide critical imaging support for percutaneous structural cardiac intervention procedures. They stand close to the patient and source associated risks from radiation. Objective: To investigate TEE operator radiation dose during percutaneous structural cardiac intervention. Methods: Key personnel (TEE operator (TEEOP), anesthetist (ANA), primary operator (OP1) and secondary operator (OP2)) wore instantly downloadable personal dosimeters (IDD) during procedures requiring TEE support. TEEOP effective dose (E) and E per unit Kerma area product (E/KAP) were calculated. E/KAP was compared to c-arm projections. Additional shielding for TEEOP was implemented and doses were measured for a further 50 procedures. Multivariate linear regression was performed to investigate independent predictors of radiation dose reduction. Results: In the initial 98 procedures, median TEEOP E was 2.62 (IQR=0.95-4.76) µSv, similar to OP1 E: 1.91 (0.48-3.81) µSv (p=0.101), but significantly higher than OP2 E: 0.48 (0.00-1.91) µSv (p<0.001) and ANA E: 0.48 (0.00-1.43) µSv (p<0.001)). Procedures using predominantly RAO and steep RAO projections were associated with high TEEOP E/KAP (**p=0.041**). In a further 50 procedures, with additional TEEOP shielding, TEEOP E was reduced by 82% (2.62 (0.95-4.76) to 0.48 (0.00-1.43) µSv (p<0.001)). Multivariate regression demonstrated shielding, procedure type and KAP as independent predictors of TEEOP dose. Conclusion: TEE operators are exposed to a radiation dose that is at least as high as that of OP1 during percutaneous cardiac intervention. Doses were higher with procedures using predominantly RAO projections. Radiation doses can be significantly reduced with the use of an additional ceiling suspended lead shield.

6. Learning Pathway (choose one of the following): Congenital Heart Disease, Acute Coronary Syndromes, Arrhythmias and Clinical EP, Stable Ischemic Heart Disease, Standard ECG, Stress Testing, Prevention, Heart Failure and Cardiomyopathies, Noninvasive Imaging, Invasive Cardiovascular Angiography and Intervention, Pericardial Disease, Vascular Medicine, Pulmonary Hypertension and Venous Thromboembolic Disease, Valvular Heart Disease
7. COMPETENCIES: ACC education staff will enter
8. CME Learning Objective:
   Upon completion of this activity, the learner should be able to:

   1. State which staff members receive the highest radiation dose during percutaneous structural cardiac intervention procedures.
   2. Compare x-ray c-arm projections and their impact on operator radiation dose.
   3. Explain why certain patient, procedural and environmental factors may affect staff radiation exposure in the cardiac catheter laboratory.

9. Quiz

A 75 year old male with persistent atrial fibrillation and is contra-indicated for anticoagulation therapy is undergoing percutaneous left atrial appendage occlusion in a cardiac catheterisation laboratory. The patient is anaesthetized and ventilated. Fluoroscopy and trans esophagel echocardiography (TEE) is being utilized for trans septal puncture and device placement. The attending team consists of an anesthetist with their assistant, a cardiologist who is operating the TEE probe, an interventional cardiologist (IC) who is inserting the occlusion device, being assisted by a fellow in training and a scrub nurse. In addition there is a second nurse present and a radiation technologist. All staff are wearing a lead apron and a lead thyroid collar. The IC is stood on the patient's right and using a lead acrylic shield that is suspended from the ceiling and a lead drape attached to the tableside for additional protection. The TEE operator is stood on the patient's left side, towards the patient's head.

Questions / Answers / Rationale:

1. Which of the following c-arm angulations is most likely to be used for the majority of this procedure?

    a. Right anterior oblique
    b. Left anterior oblique
    c. Postero-anterior
    d. Antero-posterior

2. Which of the following c-arm projections is likely to deliver a high dose to the TEE operator?

    a. Postero-anterior
    b. Antero-posterior
    c. Right anterior oblique
    d. Left anterior oblique

3. Which of the following radiation protection measures would be of benefit to the TEE operator during this procedure?

    a. Lead eye glasses
    b. An additional lead acrylic shield
    c. Changing the fluoroscopy frame rate from 10 to 7.5 pulses per second
    d. All of the above

4. Which of the following X-ray system parameters would have to most impact in radiation dose reduction to the patient and the attending staff.

    a. Reducing fluoroscopy time
    b. Reducing fluorographic (cine) acquisitions
    c. Increasing the distance between the patient and the image receptor
    d. Decreasing the distance between the patient and the X-ray source

Answers:

1. A; Left atrial appendage (LAA) occlusion has two major fluoroscopic components; trans septal puncture and device implantation. Whilst trans septal puncture is usually performed in the left anterior oblique projection

to profile the atrial septum it should use less fluoroscopy than the LAA device insertion. In addition, cine acquisition is performed whilst injecting the LAA with contrast media before and after deployment, which uses significantly more radiation than fluoroscopy.(1,2) This major component of the procedure is usually performed in the RAO projection to enable coaxial visualization of the LAA orifice for accurate device implantation. The postero-anterior projection is seldom used in these procedures, other than for vascular access. The antero-posterior projection would almost never be used as x-ray system c-arms are orientated with the X-ray tube under the table and the image receptor above the table as this reduces staff dose.(2)

2. C. The present study demonstrates that radiation dose to the TEE operator is highest when the right anterior oblique projection is used. This is due to backscatter of radiation from the patient, which has been demonstrated to be higher when the c-arm orientation is directed away from the operator. The primary catheter operator would receive the lowest dose in RAO projections but the highest dose with LAO projections.(3) LAO projections would give the TEE operator the lowest doses in this scenario. Postero anterior projections use less radiation overall due to the relative reduced thickness of the patient(2) and the backscatter is also evenly distributed to the patients left and right. The anterio-posterior projection would almost never be used for these procedures as x-ray system c-arms are orientated with the x-ray tube under the table and the image receptor above the table and this reduces staff dose.(2)
3. D; There are many ways to reduce staff dose during fluoroscopy procedures but the basic principle of keeping the radiation dose as low as reasonably achievable (ALARA) holds true.(4) Keeping the radiation dose to the minimum required reduces radiation dose to the patient and the staff. Reducing the fluoroscopy pulse rate is one way of achieving this; a reduction from 10 to 7.5 pulses per second will result in a 25% reduction in radiation dose. The addition of more shielding has been demonstrated in this study to reduce radiation dose to TEE operators and additional shielding has been demonstrated to reduce radiation dose to interventional cardiologists in other studies.(5,6) The lens of the eye has been demonstrated to be sensitive to radiation, with cataracts seen in interventional cardiologists.(7) Wearing lead eye glasses reduces the amount of radiation that reaches the eye and therefore the onset of cataracts.
4. B; Fluorographic or *cine* acquisitions produce high quality images that are stored by the X-ray system but use considerably more radiation than fluoroscopy.(1,2) Reducing fluoroscopy time will reduce the overall radiation dose but not to the degree that reducing cine acquisitions would. Increasing the distance between the patient and image receptor will increase scattered radiation received by the staff and this would also result in an automatic increase in radiation from the X-ray machine, increasing patient radiation dose. Decreasing the distance between the patient and the X-ray source would also increase the radiation dose to the patient.(2)

10. Were there any COI to resolve with any of the authors? YES_____ NO__✓___

11. References: **Note: Please try not to use any references older than 5 years old**

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