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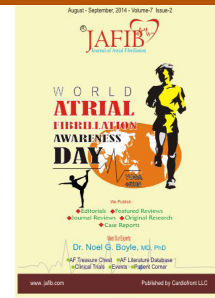

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The Growing Culture Of A Minimally Fluoroscopic Approach In Electrophysiology Lab

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Abstract

Most of interventional procedures in cardiology are carried out under fluoroscopic imaging guidance. Besides other peri-interventional risks, radiation exposure should be considered for its stochastic (inducing malignancy) and deterministic effects on health (tissue reactions like erythema, hair loss and cataracts). In this article we analized the radiation risk from cardiovascular imaging to both patients and medical staff and discusses how customize the X-ray system and how to implement shielding measures in the cath lab. Finally, we reviewed the most recent developments and the latest findings in catheter navigation and 3D electronatomical mapping systems that may help to reduce patient and operator exposure.

Introduction

Current State Of Fluoroscopy Use In Electrophysiology Labortory

As the first imaging modality of the living human body, X-ray fluoroscopic imaging has been the most important technical tool in modern medicine (Roentgen). It allowed one to see the inside of the body and, after contrast injection, even of soft tissues like the beating heart.[1] To date, most of interventional procedures in cardiology are carried out under fluoroscopic imaging guidance. Besides other peri-interventional risks, radiation exposure should be considered for its stochastic (inducing malignancy) and deterministic effects on health (tissue reactions like erythema, hair loss and cataracts).[2]

Due to increased interventional procedures and imaging studies in the last decades, patients are being exposed to a substantial amount of radiation over their lifetime. Some procedures like catheter ablation of atrial fibrillation frequently requires cardiac computed tomography (CT) scan before the intervention and more than one ablation procedure, thereby adding a substantial amount of radiation.[3] On an average, a complex cardiac radiofrequency ablation corresponds to 750 chest X-rays (range 100–2850).[4] Recently, attention has been applied to the radiation exposure of the catheter lab staff who expose themselves professionally. Being close to the patient during an interventional procedure, the first hand operator is exposed to scattered radiation, whilst other health care professionals are better protected by their position at a greater distance to the radiation source and the patient itself.[5]

Besides the associated X-ray exposure, the main limitation of fluoroscopy is that in complex arrhythmias fluoroscopy only provides two-dimensional (2D) representations of three dimensional (3D) anatomical structures as potentials targets for ablation. With the evolution of technology, new non fluoroscopic 3D mapping systems from the late 1990s have been an alternative to fluoroscopy alone in electrophysiology world. Infact constructing a virtual real time 3D map, catheter navigation is facilitated while minimizing or eliminating fluoroscopy exposure. New software upgrades to non fluoroscopic 3D mapping have resulted in very detailed cardiac chambers, potentially eliminating pre-procedure CT imaging.

In this article we analized the radiation risk from cardiovascular imaging to both patients and medical staff and discusses how to customize the X-ray system and how to implement shielding measures in the cath lab. Finally, we reviewed the most recent developments and the latest findings in catheter navigation and 3D electronatomical mapping systems that may help to reduce patient and operator

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None.

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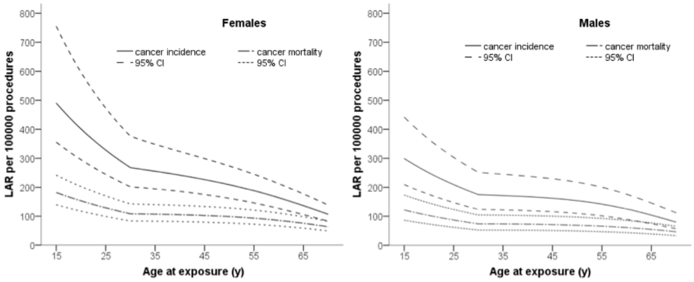

Figure 1: Lifetime attributable risk of cancer incidence (solid line) and mortality (dash-dot line) induced by radiation exposure during RFA procedure with the 95% confidence interval confidence interval (dashed lines) in function of age at exposure for females (left) and males (right), for a mean effective dose of 19.1 mSv per procedure estimated from reported literature.

exposure.

Radiation Risk Associated With Radiofrequency Catheter Ablation Procedures

How To Measure Radiation Exposure?

Fluoroscopy time and Dose Area Product (DAP) are widely used to assess the patient risk as reported by several studies, for they are rather easy to measure. Nevertheless the first is not even a dosimetric quantity, the latter, although somewhat useful to avoid skin injuries during prolonged procedures, does not take into account of specific factors such as the beam geometry with respect to the patient. Therefore none of them is adequate to estimate the patient risk. The International Commission on Radiological Protection recommends the use of the Effective Dose (ED), expressed as Sievert (Sv) or milliSievert (mSv) and usually reported as a range, to estimate the radiation detriment.[6,7] Conversely only a small number of RFA studies have reported ED estimations. Table 1 reports the studies with 10 or more patients published between 1994 and 2013 including ED estimations in their results.[8,9,10,11,12,13,14,15] The average values per single procedure felt in the range of 5.7–24.4 mSv, which correspond to lifetime attributable cancer risks of 0.02–0.1%. Such values are generally considered acceptable, although substantially higher compared to the average ED values of other radiological procedures, and may exceed 50–100 mSv in some cases of complicated or repeated procedures.

The Committee on the Biological Effects of lonizing Radiation (BEIR) proposed a method to assess the risk of cancer incidence and mortality from patient dosimetry, dependent on age at exposure and gender.[16] Figure 1 shows the estimates of life-time attributable risk (LAR) in function of the age at exposure for males and females estimated from average effective doses calculated using the values from the reported literature (19 mSv). As expected, the risks decreased with age at exposure and were higher in females. The average cancer risk was 205 cases per 100000 procedures with 89 fatal malignancy for exposure-age of 40 years. The risks were almost doubled for exposure-age of 15 years.

The EDs for medical staff are usually significantly smaller compared to patient EDs, since the radiation exposure is lower. Several studies published between 1994 and 2013[14,17,18] reported ED estimations for the medical personnel of RFA procedures. The ED values for the first operator were about 2 – 3 orders of magnitude smaller than patient EDs and average values varied between 1.8 and 65.6 μSv per procedure. Despite a significant smaller radiation exposure for operators, recent reports have hinted an excess risk of brain tumors (predominantly at the more exposed left side) and (left sided) breast cancer in female cardiologist.[19] Since the stochastic effects are cumulative, a reduction in the use of fluoroscopy would be beneficial also in reducing the burden of cumulative effective dose of the cardiologist.

DNA Damage Upon Ion Radiation: Detection In Patients And Hospital Workers

One of the major limits in assessing cancer risk in low radiation exposed patients consists in the need of a correct and precise measure of radiation-induced DNA damage. The most widely used assay to detect DNA damage is the micronucleus (MN) assay. Micronuclei are extra-nuclear bodies containing a portion of or a whole chromosome which was not carried to the opposite poles during cell division. Their formation results in the daughter cell lacking a part of or a whole chromosome. After cellular aberrant separation, micronuclei normally develop nuclear membranes and form as a third small nucleus. Severe genetic damage can lead to the formation of more than one micronucleus.

MN assay has been used by Andreassi et al. in one of the first studies regarding DNA damage in patients undergoing cardiovascular procedures.[20] In particular, the researchers performed chromosomal damage analysis in 72 patients undergoing invasive interventions such as: coronary angiography, percutaneous coronary intervention, transluminal angioplasty and cardiac resynchronization therapy. MN frequency evaluation after 2 and 24 hours post intervention showed a significant rise in DNA damage. In a similar study, MN assay was used to assess the entity of radiation induced genetic aberrations in 18 out of 59 children with complex congenital diseases undergoing cardiac catheterization procedures. As in the previously cited study, Ait-Ali and coworkers showed a significant increase in MN formation as soon as 2h after procedures, a result clearly hinting to a great need for strict radiation dose optimization in particular in patients of young age and with a long life expectancy.[21]

Recently, additional markers to estimate radiation induced DNA damage have been proposed and investigated. In particular, γ-H2AX foci immunodetection have been described as a useful and quantitative biomarker of low-level radiation exposure.[22] This assay relies on the fact that ionizing radiation induces DNA double strand breaks (DSB) and, in turn, activates histone H2AX within 3 minutes after DNA damage, via phosphorylation of Ser 139;[23] this particular phosphorylated form of H2AX tends to form foci and seems to be essential for the DNA damage repair, in addition to having been demonstrated to be directly proportional to damage extent (1 focus = 1 DNA DSB).[24] This assay has been used in a recent work by Beels at al. to detect and quantitate DNA damage in pediatric patients undergoing cardiac catheterization; the investigators demonstrated a net increase in γ-H2AX foci after the procedures, again showing the importance of radiological awareness to minimize the possible long term oncogenic effects of x-ray exposure.[25] Beside currently used assays, which are able to directly detect DNA damage induced upon irradiation, some new possible biomarkers are being currently proposed to increase the reliability of risk assessment for both patients and hospital operators. Indeed, risk assessment based on DNA damage in hospital workers exposed to ionizing radiation has been the subject of numerous studies in the past, and both MN and Comet assays have been employed.[26,27,28,29] Comet Assay (the nickname for

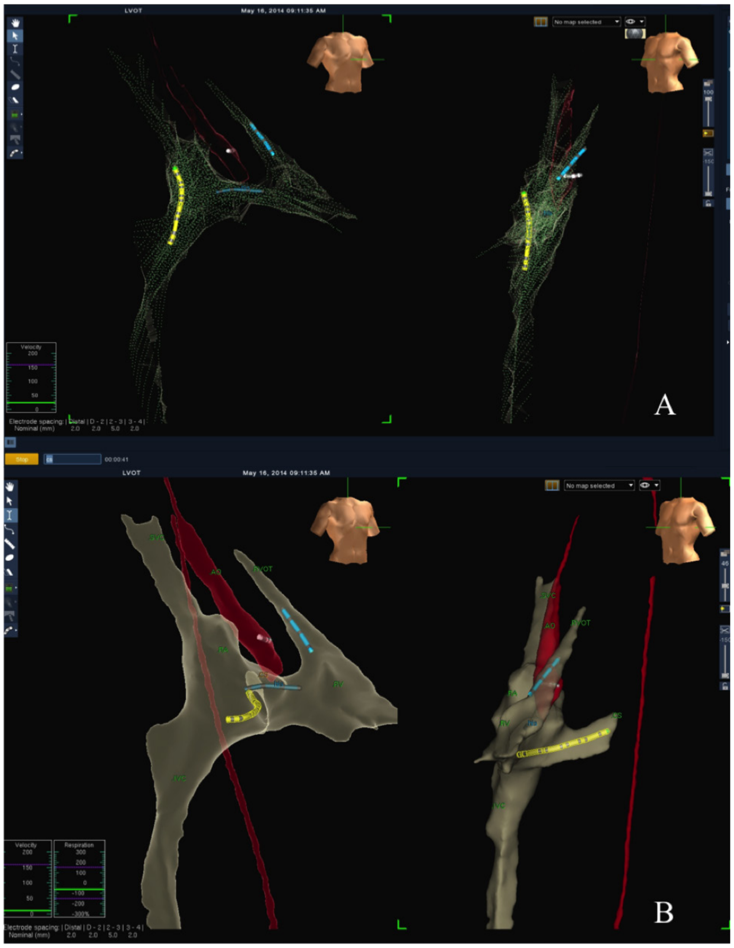

Figure 2: Panel A: Catheters were placed from the right femoral vein and advanced up to inferior vena cava to the right atrium and confirmed by the presence of atrial electrograms. On the left RAO view; on the right LAO view. Panel B: typical, full right sided geometry as drawn by Ensite System. On the left RAO view; on the right LAO view. IVC: inferior vena cava; RA: right atrium; RV: right ventricle; RVOT: right ventricle outflow tract. AO: ascending aorta.

single-cell gel electrophoresis) is a simple method for measuring deoxyribonucleic acid (DNA) strand breaks in eukaryotic cells. Cells embedded in agarose on a microscope slide are lysed with detergent and high salt to form nucleoids containing supercoiled loops of DNA linked to the nuclear matrix. Electrophoresis at high pH results in structures resembling comets, observed by fluorescence microscopy; the intensity of the comet tail relative to the head reflects the number of DNA breaks.

All these studies evidenced a long term effect on circulating cells of exposed hospital workers, with a possible role for smoke as additional risk factor.

In a recent work by Andreassi et al, a new approach consisting in the association of single nucleotide polymorphisms (SNPs) in DNA repair genes with MN assay demonstrated that genetic predisposition seems to increase chromosomal DNA damage levels in interventional cardiologists.[30] Lately, new possible molecular markers of DNA damage in endothelial and blood cells have been discovered that could lead to the introduction of new sensitive and rapid assays to detect and quantify the negative effects of ionizing radiations.[31,32] In their study, Barjactarovic and coworkers investigated the effects of low-dose gamma radiation on the proteome of coronary artery endothelial cells cultivated in vitro, showing a significant deregulation in the expression of 28 proteins. Interestingly, the same study evidenced radiation induced alterations in the levels of 2 microRNAs, miR-146b and -21, the latter being putatively able to target 3 out of the 28 radiation-modulated proteins (Desmoglein 1, phosphoglyceratemutase and target of Myb protein 1).

Transcriptional regulation in ex-vivo irradiated cells was the focus of investigation of Manning and colleagues in a recent study showing that both low and high doses of ionizing radiations can modulate the expression of specific genes. In particular, the researchers showed a dose response effect in the levels of 13 genes that were modulated after 2 and/or 24 h post cells irradiation.

The possible limit of these new approaches consists in the lack of data on their possible application for long term cancer risk assessment.

The Growing Culture of Radiation Protection

Since Vaseline To 3D Technology

Within 12 months of the Röntgen"s discovery of X rays in 1895, papers appeared in the literature reporting adverse effects from high exposure. Just 1 year after, the American engineer Fuchs gave what is generally recognized as the first protection advice: a) make the exposure as short as possible, b) do not stand within 30 cm of the X-ray tube, and c) coat the skin with Vaseline and leave an extra layer on the most exposed area. Thus, within 1 year of dealing with radiation, the three basic tenets of practical radiological protection – time, distance, and shielding – had been established. Gradually, the need of radiation protection led to the foundation of a protection committee, established at the second International Congress of Radiology in Stockholm in 1928. While initially, radiation protection aimed to avoid visible and early effects after prolonged exposure to radiation, subsequently the rules on radiation exposure were formulated to prevent late harmful effects such as cancer induction. Indeed, most of the information available on the effects of radiation exposure in humans was based observing the survivors of the Hiroshima and Nagasaki bombings.

ALARA - As Low As Reasonably Achievable - is the safety principle designed to minimize radiation doses received by radiation workers using practical, cost-effective measures. The ALARA assumption is that there is no measurable dose of radiation that can be considered safe. Radiation dose and its biological effects on living tissues are modeled by a relationship known as "linear-no-threshold" risk model. Every radiation dose of any magnitude can produce some level of detrimental effects that may include increased risk of genetic mutations and cancer.

With the interest in minimizing radiation dosage, a variety of alternative approaches were investigated to provide guidance in the interventional cardiology laboratories. Three-dimensional non fluoroscopic mapping systems have revolutionized the "way-to-do" of EP operators.[33,34,35,36] The most commonly used are the CARTO®system (Biosense Webster, Inc., Diamond Bar, CA, USA) and the EnSiteNavX system (St. Jude Medical, Inc., St. Paul, MN, USA) (Figures 2-5). In addition, a new system, the Rhythmia™ mapping system (Rhythmia Medical, Burlington, MA, USA), has been recently developed and introduced in clinical practice. Briefly, the principle of catheter navigation with the CARTO® mapping system is magnetic-field whilst the NavX technology works with impedance-based measurements (electrical field). These technologies allow to accurately determine the location of arrhythmia origin, define cardiac

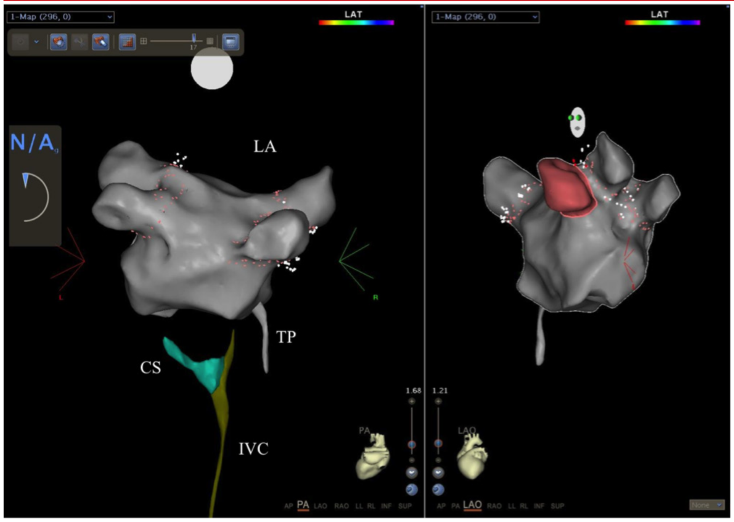

Figure 3: Left atrium (gray), inferior vena cava (green) and CS anatomy (blue) as drawn with CARTO System. On the left PA view; on the right LAO view.
IVC: inferior vena cava; CS: coronary sinus; LA: left atrium; TP: transeptal puncture.

chamber geometry in 3D, delineate areas of anatomic interest, and allow catheter manipulation and positioning without fluoroscopic guidance. Later versions of these mapping systems have allowed the fusion with MRI image or CT scan (Figure 4) and significant reduction in fluoroscopy exposure was demonstrated.[37,38] Another extension to the CARTO mapping technology enabling ultrasound integration was the CARTOSound (Figure 4). It creates a 3D image of a specific heart chamber undergoing cardiac ablation by utilizing an intracardiac ultrasound catheter.[39,40] The competition between these systems has led to a "mapping race"resulting in the systems developing increasingly similar characteristics including the ability to visualize multiple non-proprietary catheters.

A new sensor-based non fluoroscopic approach, developed by MediGuide and St Jude Medical, is recently entered in the market. Clinical application of the gMPS technology in electrophysiology revealed feasibility of non fluoroscopic catheter visualization within the work flow of conventional invasive diagnostic EP procedures with significant reduction in X-ray exposure up to 80% especially for the treatment of complex arrhythmias.[41]

The innovative CARTOUnivu module provides for fixed fluoroscopic images or cines to be transferred to the 3-D electro-anatomic mapping system. The module allows real-time visualization of intracardiac catheters against a background of a stored fluoroscopic image (Figure 2). Typically, multiple fluoroscopic images (three to eight) are acquired at different angulations and stored. Once transferred, the fluoro image is integrated into the 3-D map view, allowing the user to create an electroanatomical map on top of the captured fluoroscopic image or looping cine. Not only does this proved fluoroscopic images for reference, electrophysiologists consistently commented that it diminished the interest in confirming catheter location with additional fluoroscopy. In a non-randomized retrospective study, researchers found a statistically significant reduction in fluoroscopy times and in dosages for EP ablation procedures utilizing the CARTOUnivu module fluoroscopic integration system.

Echocardiography

Intracardiac echocardiography (ICE) allows to obtain detailed imaging of cardiac structures from within the vascular system, using a transvenous ultrasound probe placed in the right heart, reducing fluoroscopy times and doses. These catheters have been extensively used in order to guide transseptal catheterization.[42,43] Moreover, ICE helps to define the anatomy of the left atrium, pulmonary veins and visualize target structures during EP procedures.[44,45] In addition, it is possible to visualize the lesion site and formation, such as swelling and crater formation and to promptly identify possible complications such as occurrence of microbubbles, clot formation and pericardial effusion.[46] Real-time 3D transesophagel echocardiography (TEE) can be used as an alternative to ICE. However, post-acquisition image processing is time-consuming and general anesthesia with endotracheal intubation is required in all patients.[47,48]

Rotational Angiography

Recently, 3D rotational angiography (DynaCT, Siemens) has been introduced as an intraoperative modality for 3D imaging during cardiac ablation. In 3D rotational angiography (3DRA), the C-arm typically performs a 200° rotation around the patient. A large number of 2D projections are acquired over the course of the rotation. Reconstruction algorithms construct these into 3D images by volume or surface rendering. With adequate contrast agent administration and cardiac motion reduction, the image quality delivered by 3DRA has been shown to be comparable to or even exceeding classical cardiac computerized tomography.[49,50] This technique also reduces the economic impact due to additional expensive imaging studies. Moreover, 3DRA images are more likely to represent the true anatomy than a remotely acquired image, such as CT scan or MRI image, because of factors like the patient"s breathing and heart motion.[51]

Remote 3D Magnetic Navigation Systems and Robotic Catheter System

The use of remote navigation systems could systematically decrease clinician fatigue and fluoroscopy exposure. Currently there are two remote systems: the NiobeStereotaxis Magnetic Navigation System (Stereotaxis, Inc., St Louis, MO) and the Hansen Sensei Robotic Catheter System (Hansen Medical, Mountain View, CA). Both systems allow the physician to perform the mapping and ablation procedure while sitting in a control room remote from the patient (Figure 7).

The Niobe Stereotaxis Magnetic Navigation System (MNS) operates by using two large permanent magnets placed on either side of the patient that create a magnetic field inside the chest of the patient in which a catheter with magnetic tip, 7-F 3.5-mm-tip floppy irrigated catheter (Navistar RMT), can be moved in the desired directions, just modifying the magnetic field using a joystick in the control room, and used for mapping and ablation. In addition, the system includes a dedicated 3D EAM system (CARTO RMT). Significant disadvantages of MNS are the extremely high cost of the system itself and the need of a dedicated EP laboratory properly shielded.[52,53,54] Focusing on fluoroscopy times and radiation doses, different groups reached a significant reduction in fluoroscopy time and in radiation dose.[55,56,57]

The Hansen™ (Hansen Medical Inc., Mount View, CA) Robotic system is a flexible, robotic platform that combines 3D catheter control and visualization. The hand motions applied at the workstation are transferred to the catheter inside the heart of the patient. The major advantage is that once the catheter reaches the target site the robotic hand guarantees an extremely stable position. In addition, the IntelliSense™ technology provides the information about how much pressure is being exerted by the catheter. The Hansen system

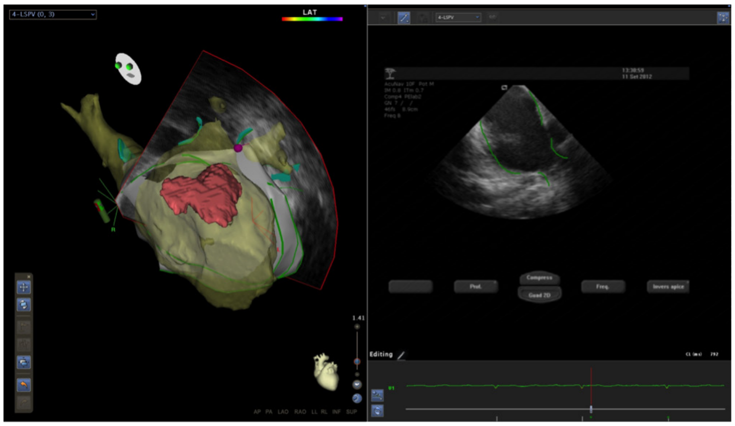

Figure 4: Screen shot of the CARTO system. On the left, intracardiac echocardiography (ICE) 2D image of the left atrium (LA), left superior and left inferior pulmonary veins. The green lines represent the endocardial borders. On the right, co-registration of the LA ICE 3D anatomical shell and preoperative cardiac CT scan

does not require a dedicated 3D EAM system, but is equally compatible with CARTO and NavX systems.[52] Since the preliminary human experience published in 2008, the robotic navigation system has been shown to be safe and feasible, with similar results compared with the manual approach, and to significantly reduce radiation exposure.[53,54,58,59]

Radiation Protection Tools

Despite the wide use of 3D EAM, ultrasound-guided procedures and remote catheter navigation, X-ray technology is still the most commonly utilized technique for medical imaging. The greatest source of X rays to the operator and staff is scatter from the patient. Chronic radiation exposure in the work place requires the use of protective tools in order to limit occupational radiation dose to an acceptable level. The purpose of radiation protection tools is to improve operator and staff safety without impeding the procedure or jeopardizing the patient"s safety. There are different tools currently available for radiation protection in the electrophysiology laboratories: architectural shielding, equipment-mounted shields, personal protective devices, personal mobile shields and radiation protection units.[60,61]

Architectural shielding is built into the walls of the EP laboratory. In addition, rolling and stationary shields, constructed of transparent leaded plastic, are available and are useful for providing additional shielding for both operators and staff.[62]

Equipment-mounted shielding includes tables-suspended and ceiling-suspended shields. It has been shown to substantially reduce the operator"s dose. Table-suspended shielding are drapes positioned between the X-ray tube and the operator from the side of the patient table. Unfortunately, they are ineffective when the C-arm is in oblique or lateral position. Ceiling-suspended shielding are leaded plastic shields positioned between the operator face and the X-ray detector.[63,64]

Personal protective devices include aprons, thyroid shields, eyewear, and gloves. Protective aprons with thyroid shields are the principal radiation protection tools for interventional workers. More advanced equipment also includes lead caps. According to regulations, it is necessary the use of apron of at least 0.5 mm lead equivalent thickness. Transmission of 70-100kVp X-rays through 0.5 mm lead ranges from 0.5 to 5%.[65] Effective personal protective devices use is expected from every staff member in order to maintain the radiation dose to less than 20 mSv/y, averaged over a 5-year period, according to current recommendations of International Commission on Radiation Protection.[66]

The RADPAD (Worldwide Innovations & Technologies, Inc., Kansas City, KS) is a Bismuth-made, disposable, sterile, lead-free surgical drape. Being positioned on the patient, it has been shown to reduce scatter radiation, in particular during complex device implantation.[67,68]

The radiation protection units have been developed to reduce the development of long-term orthopedics problems such as aches and pains in the neck, back, hips, knees and ankles that ranges in severity.[69,70] Cathpax (LemerPax, Carquefou, France), a radiation protection cabin, was developed as alternative protection apparel.[71] It uses 2 mm lead-equivalent walls, including transparent leaded plastic in its upper parts, to surround the operator on two sides and from above. This unit is mobile, adjustable in height, and is prepared with specifically designed drapes to provide sterile patient access. ZeroGravity (Zgrav, CFI Medical Solutions) is an entirely suspended radiation protection system. It is made of a suspended lead apron covering the operator from head to calf excluding right arm and left forearm.[72] Recently, Fattal and Goldstein described the first in man clinical use of a complete barrier radiation unit - Trinity System (ECLS, Salt Lake City, UT).[73]

Use Of Non-Fluoroscopic Guiding Technology In Order To Obtain A Minimally Fluoroscopic Approach

In the last few years several papers and case-reports have been published showing the feasibility and safety of a totally non fluoroscopic approach using mapping system principally as navigation system in order to move the catheters through the vessels and the heart chambers.

Below the main studies that have used a minimally fluoroscopic approach thanks to the navigation/mapping systems in different setting of patients.

Pediatric Population

While minimizing fluoroscopy is prudent for everyone, children are at an increased risk from radiation exposure because they are growing and have a longer life expectancy.[74] Children receive also a greater effective dose as scatter radiation has a shorter distance to travel to reach sensitive organ such as the bone marrow, liver and breast tissue.[75] For these reasons children are more susceptible to the risk of radiation-induced carcinogenesis and decreasing fluoroscopic exposure during electrophysiologic ablation procedures gives them a greater benefit compared with adults.[76] Among the pediatric population, children with congenital heart disease are at an even higher risk. Owing to anatomic alterations and multiple substrates, procedures are often longer than in patients with structurally normal hearts and they are likely to have multiple procedures.

With increasing operator experience, fluoroscopy times decreased from nearly an hour in 1991-1992, to 40 min in 1995-1996 and to 36 min in 2004.[77,78,79]

Ablation of supraventricular tachycardia is the most common procedure performed in children and first experiences in reducing fluoroscopy exposure were performed in this subset. Drago et al. in 2002 described for the first time the feasibility and efficacy of minimal-fluoroscopy ablation of right-sided accessory pathways using the CARTO three-dimensional navigation system in children with normal heart anatomy.[80] Starting from this first experience, in the

Figure 5: On the left: Inferior vena cava, right atrium and right ventricle outflow tract geometry as drawn with Ensite System. AP view. On the right: typical: right ventricle outflow tract (green) geometry as drawn by Ensite System. LAO view. White dots represent ablation point during of catheter ablation of frequent premature ventricular complexes arising from right ventricle outflow tract.

following years others studies have been published, investigating the feasibility of a minimal-fluoroscopic approach in almost all kinds of electrophysiologic procedures in children. In 2006 Papagiannis et al. described their experience with NavX for the ablation of atrio-ventricular re-entrant tachycardia and both right and left-sided accessory pathways. They included also children with congenital heart disease, showing no significant differences in success rate.[81] In 2007 Papez et al. and Smith et al. confirmed the feasibility and efficacy of the ablation of atrioventricular re-entrant tachycardia and atrioventricular nodal re-entrant tachycardia with LocaLisa and NavX system, respectively.[82,83] Smith et al. used no fluoroscopy in 80% of the procedures and pointed out that the most common reason for fluoroscopy use was the need to perform a transseptal puncture. In 2007 it was also described for the first time a case series of right-sided catheter ablation with cryo-energy and minimal-fluoroscopy.[84] It was in 2008 when the first series of transseptal puncture have been performed without fluoroscopy, thanks to the combination of trans-esophageal echocardiography and NavX guidance.[85]

Intracardiac echocardiography was introduced as a tool to reduce fluoroscopy exposure in 2010 when Kean et al. reported their experience with CARTOSound in treating different kinds of arrhythmia. They included also children with congenital heart disease.[86] The sub-population of children with congenital heart disease has been better investigated in 2011 by Papagiannis et al. They compared two groups of patients, one group undergoing fluoroscopic only ablation and the other one using NavX non-fluoroscopic navigation system. They performed a sub-analysis of children with congenital heart disease and observed that the reduction in fluoroscopic exposure with the use of the NavX system was preserved in this population.[87]

If previous described studies are retrospective studies, it was Miyake et al. in 2011 that performed the first prospective, controlled, single-centre study of ablation of supraventricular tachycardia among children, randomizing to fluoroscopy (control group) or fluoroscopy + AcuNav intracardiac ultrasound + NavX electroanatomic mapping (study group). The success rate was 97% in the control group and 100% in the study group without differences in adverse events. Non-fluoroscopic imaging reduced median fluoroscopy time by 59% (18.3 minutes vs 7.5 minutes, $P<0.001$) and radiation exposure by 72% (387 vs 110 mGy, $P<0.001$).[88] A second prospective, controlled, single-center study was published in 2013 and randomized to intra-cardiac echocardiography plus electroanatomic mapping or electroanatomic mapping only in children with normal cardiac anatomy performing ablation for supraventricular tachycardia. The use of intra-cardiac echocardiography reduced the fluoroscopic exposure for transseptal puncture .

As a consequence of growing experience with non-fluoroscopic navigation systems, also accessory pathways in close proximity to the normal conduction tissue and arrhythmia other than supraventricular tachycardia have been successfully ablated with minimal- or no-fluoroscopy.[89] In 2011 it was described a small series of children that underwent ablation of ventricular arrhythmia using electroanatomic mapping with 3D EnSiteNavX system. No fluoroscopy was used in patients with right-sided arrhythmia, while the two patients with left-sided arrhythmia had 1.0 and 1.9 minutes of fluoroscopy. Small amounts of radiation may be required for evaluation of coronary arteries or other anatomic substrates.[90] Last year the utility and safety of the NavX system in reducing fluoroscopy exposure during ablation of ventricular tachycardia was confirmed in a larger series of children.

There is a growing body of literature that demonstrates safety and efficacy of minimal or no-fluoroscopic use in pediatric patients undergoing ablation procedures by using electroanatomic mapping systems. In most studies, this has been accomplished without extending procedure times. However, the use of electroanatomic mapping systems increases the cost of the procedures over fluoroscopy alone and requires a great experience.[91] The extent to which long-term benefits outweigh the increased costs remains actually unknown. The publication of the NO-PARTY trial, the only one multi-centre, randomized controlled trial up to now, will probably give an answer to the cost-effectiveness of non-fluoroscopic radiofrequency catheter ablation, in addition to confirmation of the reduction of radiation exposure to the patient and to the operator and feasibility and safety of these procedures.

Adult Population

In contrast with the pediatric population, the greater number of procedures performed in the adult population allowed prospective-randomized trial to have been published since 2000. Kottkamp et al. where the first ones that randomized 50 patients with typical atrial flutter to receive isthmus ablation using conventional fluoroscopy for catheter navigation (group I, n=24) or electromagnetic mapping (group II, n=26). They demonstrated that electromagnetic mapping permitted a high significantly reduction in exposure to fluoroscopy (22.0 ± 6.3 min in group I and 3.9 ± 1.5 min in group II; $P<0,0001$) reducing the exposure to levels anticipated for diagnostic electrophysiologic studies. The efficacy was maintained high in both groups . In 2003 Schneider et al. confirmed these findings in a series of 50 patients randomly assigned to undergo radiofrequency ablation of typical atrial flutter guided by a conventional fluoroscopy-based approach or by the LocaLisa system.[92] The efficacy and safety of electroanatomic mapping for the reduction of radiation exposure during ablation of typical atrial flutter was than reaffirmed in a larger series of patients in 2009 by Hindricks et al.[93] They randomized a total of

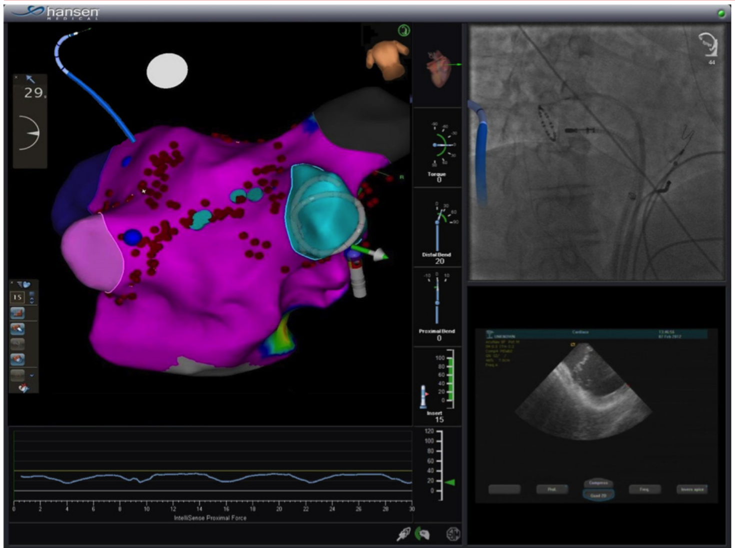

Figure 6: The robotic Sensei X system (Hansen Medical,CA) screen shot. On the left, left atrium as drawn with CARTO System. Upper right, fluoroscopy view. Bottom right, intracardiac echocardiography.

210 patients with documented typical atrial flutter to conventional ablation strategy or electroanatomically guided mapping and ablation (CARTO). The success was not significantly different between the two groups, but the fluoroscopy exposure time was reduced by almost 50% in the electroanatomically guided ablation group (7.7 ± 7.3 min vs 14.8 ± 11.9 min; P<0,05). Of course, the cost of the procedures was higher in the study group (USD 3,870 vs USD 2,720).

In 2005 it was published the first randomized trial of reduction of fluoroscopic exposure in atrial fibrillation ablations. Seventy-two patients were randomized to ablation with or without non-fluoroscopic navigation. The target of pulmonary vein isolation was achieved in all patients and fluoroscopy was significantly reduced in the study group (15.4 ± 3.4 min vs 21.3 ± 6.4 min; P<0,001), demonstrating for the first time the feasibility and efficacy of minimal-fluoroscopic ablation for atrial fibrillation.[94]

Two prospective-controlled trials add themselves to the evidence of the feasibility of reduction of radiation exposure in the electrophysiologic field, one in paroxysmal or permanent atrial fibrillation and the other one in atrioventricular nodal re-entrant tachycardia.[95,96]

Besides these prospective-randomized and prospective-controlled trials that demonstrate the feasibility and efficacy of a minimal-fluoroscopic approach, some observational studies have been published showing the chance to perform ablations completely without fluoroscopy. In 2009 Ferguson et al. published a series of 21 patients that underwent ablation for atrial fibrillation. In 19 of them no fluoroscopy was used thanks to the use of intra-cardiac echocardiography and electroanatomic mapping navigation also for the transseptal puncture.[97] The utility of the combination of intra-cardiac echocardiography and electroanatomic mapping was then confirmed in 2010 by Reddy et al. They evaluated this combination in 20 patients undergoing pulmonary vein isolation for paroxysmal atrial fibrillation and observed that a completely fluoroless catheter ablation is safely feasible.[98] Once it has been demonstrated that also the transseptal puncture could be performed safely without fluoroscopy, it is almost obvious that ablation of common atrial flutter, atrioventricular nodal re-entrant tachycardia and accessory pathways could be free from radiation exposure too.[99,100]

In the adult population, thanks to the wide use of a minimal- or no-fluoroscopic approach in the last years, it has been possible also a comparison between different non-fluoroscopic navigation systems in term of reduction of radiation exposure. In 2006 Earley et al. randomized a total of 145 patients to a procedure guided by CARTO, Ensite NavX, or conventional mapping. Arrhythmias treated were typical atrial flutter, atrioventricular nodal re-entrant tachycardia and atrio-ventricular re-entrant tachiycardia. Overall procedure time, immediate and short-term success, complication rate, and freedom from symptoms at follow-up were identical for all groups. NavX led to the least X-ray exposure (NavX vs conventional, median: 4 vs 13 min; NavX vs CARTO, median: 4 vs 6 min), especially when NavX was used for atrio-ventricular nodal re-entrant tachycardia or typical atrial flutter.[101] A comparison between CARTO-Merge and CARTO-XP was performed in 2010 in a randomized study in patients undergoing catheter ablation for paroxysmal and persistent atrial fibrillation. Image integration using CARTO-Merge shortened the X-ray exposure (28.8 ± 14.3 min vs 58 ± 8.7 min), though not improving significantly the clinical outcome.[102] Finally, in 2012 CARTO 3 was compared with CARTO-XP in an observational study in patients treated for drug refractory atrial fibrillation. The use of the CARTO 3 system allowed a significant reduction in fluoroscopic exposure (15.9 ± 12.3 min vs 26 ± 15.1 min; P<0.001).[103]

Pregnant Women

An increased incidence of maternal cardiac arrhythmia is observed during pregnancy both in women with normal cardiac anatomy and women with structural heart disease. In most cases no treatment is necessary but occasionally arrhythmia becomes a significant clinical problem. Sustained arrhythmia can result in impaired blood flow to the fetus and fetal and neonatal adverse events are described in the literature, such as prematurity, respiratory distress syndrome, and small fetus for gestational age.[104]

Though anti-arrhythmic drugs should be the first line therapy, both the ACC/AHA and the ESC guidelines consider radiofrequency ablation as a treatment option in case of drug-refractory and poorly tolerated tachycardia (IIbC).[105,106] Due to high radiation exposure, ablation should be postponed to the second trimester if possible, and it should be performed at an experience ablation centre with suitable lead shielding and maximal use of echo- and electro-anatomic mapping systems.

Table 1: Mean effective doses in RFA procedures reported in previous studies

Study	N patients	Effective dose (mSy)
Wielandts et al.(2010)[a]	42	6.59
Perisinakis et al. (2001)[b]	24	5.67
Efstathopoulos et al. (2006)[b]	24	15.2
McFadden et al. (2002)[b]	50	17.0
Broadhead et al. (1997)[b]	81	17.3
Rosenthal et al. (1998)[b]	859	21.3
Lickfett et al. (2004)[b]	15	24.4
Macle et al. (2003)[b,c]	43	1.11

[a]Ed calculated using tissue weighting factors from ICRP 103.
[b]ED calculated using tissue weighting factors from ICRP 60.
[c]ED values reported by Macle et al. are based on measurements from a single electronic dosimeter which was likely not positioned consisently in the X-ray beam, thus ED are probably underestimated.

Supraventricular tachycardia is the most common sustained arrhythmia during pregnancy.[107] The incidence of supraventricular tachycardia complicating pregnancy has been estimated to be between 13 and 24 in 100000.[108] Atrioventricular nodal re-entrant tachycardia and atrioventricular reciprocating tachycardia are the more common forms, but incessant focal atrial tachycardia is particularly challenging as anti-arrhythmic drugs are relatively ineffective.

Experience in pregnant women derives exclusively from case reports or case series, involving women at any gestational age. All of them showed that ablation of supraventricular tachycardia with minimal- or no-fluoroscopic use is feasible and safe. No complication for the fetus was observed in any study.[109,110]

Besides supraventricular tachycardia, during pregnancy it has been observed an increased risk of electric storm due to hormonal and autonomic imbalance.[111] The incidence of electric storm in patients with ARVD/C is reported to be up to 20%, requiring effective radiofrequency ablation.[112] Current guidelines recommend metoprolol, sotalol and intravenous amiodarone for prevention of recurrent ventricular tachycardia in pregnancy, but radiofrequency ablation should be considered as a therapeutic option in selected cases.[113] Last year it was reported a case of successful rescue ablation of recurrent electric storm in a 26-year-old woman during her first pregnancy (23rd week). The ARVD/C was diagnosed 3 years earlier. Several drugs failed to control recurrences of ventricular tachycardia and radiofrequency ablation was performed on the day of the third electric storm, obtaining the resolution of the arrhythmia. The use of electro-anatomic mapping allowed a very low X-ray exposure (90 sec, 10 Gycm2). Three months after ablation, a healthy girl was delivered without any complications and during 12-months follow-up there were no recurrence of ventricular arrhythmia.[114]

Radiofrequency ablation is a highly successful procedure but it has rarely been performed during pregnancy because any X-ray exposure can be potentially harmful to the fetus. However, there are some cases in which radiofrequency ablation is the last resort solution and should be performed without hesitation to preserve two lives, the mother and the fetus one. Anyway, new non-fluoroscopic navigation systems allow performing ablation procedures with a very small amount of radiation or even without any radiation use. Considering that significant fetal complications are known to occur when exposure rates exceed 50 Sv,[115] the low-level radiation exposure showed in literature gives the chance to safely perform ablation procedures also in pregnant women affected by incessant arrhythmia and in a gestational age when delivery is not possible.[116] In future cases, it could be useful to place dosimeters on the maternal fundus under the shield to better estimate fetal exposure.[117]

Conclusion:

An underappreciated silent complication of catheter ablation procedures is radiation exposure. X-Ray exposure results in acute complications related to dose and time dependent exposure as well as a cumulative, lifetime risk to not only the patient but also the operator and electrophysiology staff. On an average, a complex cardiac radiofrequency ablation corresponds to 750 chest X-rays (range 100–2850). A reduction of the occupational and the procedural doses by a factor of 10 to even 100 can be achieved simply by a radioprotection training programme. There are many avenues to reduce the radiation exposure through system and workflow adaptations and through the use of non-fluoroscopic imaging techniques. It is hoped to witness a new era of treating arrhythmias with a minimally fluoroscopic approach.

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