Use of IV contrast media in radiotherapy planning CT scans: A UK audit

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Introduction

One of the inherent issues of computerised tomography (CT) versus magnetic resonance imaging (MRI) is the lack of soft tissue definition available in CT imaging [(1)]. Use of intravenous (IV) contrast injected directly into the patient's vein immediately prior to the radiotherapy planning (RTP) CT scan allows enhanced visualisation of target volumes and adjacent organs at risk; making delineation of radiotherapy target volumes and organs at risk easier and more accurate [(1)].

The extent of administration of intravenous (IV) contrast media within RTP CT is largely undefined. The Royal College of Radiologists (RCR) (2004)[(2)] report advised IV contrast for specific tumour sites:

Eight *recommended* tumour sites		
Pharynx	Neck Nodes UKP	Lung
Oesophagus	Stomach	Pancreas
Cholangiocarcinoma	Liver	

Twelve *suggested* tumour sites		
Salivary gland	Cervix	Hodgkin's Lymphoma
Kidney	Endometrial	Non- Hodgkin's lymphoma
Adrenal	Vulva	Rectum
Colon	Bladder	Larynx

Table 1. Recommended and suggested tumour sites RCR (2004)[(2)]

In 2010, and updated in 2015[1], further national guidelines were released identifying standards of administration [(3)]. The key points from these guidelines included:

- Risk factors should be assessed for all patients prior to IV contrast administration
- eGFR should be assessed for all non-emergency patients, a minimum eGFR of >60 ml/min/1.73m^2 is recommended.
- Metformin should not be stopped unless eGFR is <60 ml/min/1.73m^2 and in consultation with the referring clinic.
- Cannulas should be left in situ for at least 30 minutes post injection for all high risk patients.
- All centres should have treatment guidelines for reactions including extravasation.

The benefits of using IV contrast are well acknowledged [(1,2,4)] with many radiotherapy clinical trials requiring its use to aid target volume delineation and enable tumour visualisation.

Currently no standardised UK guidelines exist with respect to IV contrast protocols specific to radiotherapy planning where requirements in enhancement are often different to diagnostic studies. Many small single centre studies have investigated single aspects of contrast delivery and protocols.

[1] At the time of the audit the updated 2015 guidance had not been released. Nine recommended standards are now specified however these were not included in the original audit

However, none of the studies look at the full range of IV contrast administration practice. Anecdotal evidence suggests departmental protocols may be derived from diagnostic CT protocols; these may be outdated or inappropriate for current RTP requirements. Given the pace at which planning techniques have developed and now rely on enhanced visualisation for delineating planning target volumes and identification of organs at risk, it is pertinent to conduct a full assessment of practice to ensure optimal protocols are utilised. This audit aimed to assess which protocols are followed by individual radiotherapy departments and also consider whether RCR guidelines (2004, 2010)[2,3] are sufficient for current practice or reflective of current research and knowledge.

Materials and Method

Design

A comprehensive electronic questionnaire was sent to all 80 UK cancer centres, both qualitative and quantitative questions were used to promote objectivity and reduce researcher bias. The content and design of the questionnaire was based upon previous national studies of IV contrast administration [4,5]. Prior to distribution a pilot study of 5 randomly selected centres was performed to ensure the responses could be analysed in relation to the study questions and verify that the phrasing of the survey questions was appropriate and unbiased. No changes were identified following the pilot study. Closed, open and Likert Scale questions were used to allow analysis of protocols and opinions relating to IV contrast use and implementation.

Participants

Contact details for each radiotherapy centre were identified from the Society and College of Radiographers (SCoR) website. Stakeholders for the purpose of this evaluation were a single named representative identified by the head of department who had appropriate knowledge and experience of their own departmental protocols. Participants were advised that participation was voluntary and that by completing the questionnaire they were consenting to participate in the audit.

A four week data collection period was determined for the study, after two weeks the primary researcher re-sent the questionnaire link to the centres who had not yet responded.

Data analysis

Descriptive statistics were utilised to collate and analyse results. Data was exported to Microsoft Excel 2010 to facilitate production of graphs.

Governance Approval

The audit was approved by the host institutions internal audit committee and Sheffield Hallam University. No ethics approval was required due to the nature of the audit.

Results

In total 83% of centres responded (n=66/80), no response was received from 17% (n=14/80) of centres. There were 10% (n=8) partial responses which were excluded prior to data analysis due to a high level of unit non-responses. However, it is not known if these centres were true non-responses or if they re-started the questionnaire under a new submission as demographic data was not

collected until the end of the survey. Of the 66 responding centres 5% (n=3/66) were not operational, 5% (n=3/66) did not use IV contrast and 12% (n=8/66) were duplicated results where only one questionnaire was received that applied to a main and satellite centre, these were counted as overall responses but excluded from analyses due to repetition. Resulting in a total of 52 responses

RCR Guidelines:

Of the 52 responding centres that use IV contrast for radiotherapy planning, 98% (n=51) used it routinely.

Ninety two percent (n=48) of respondents were fully aware of RCR (2004)[2] and RCR (2010)[3] guidelines, the remaining 8% (n=4) stated they were aware the guidelines existed but were unsure of the content.

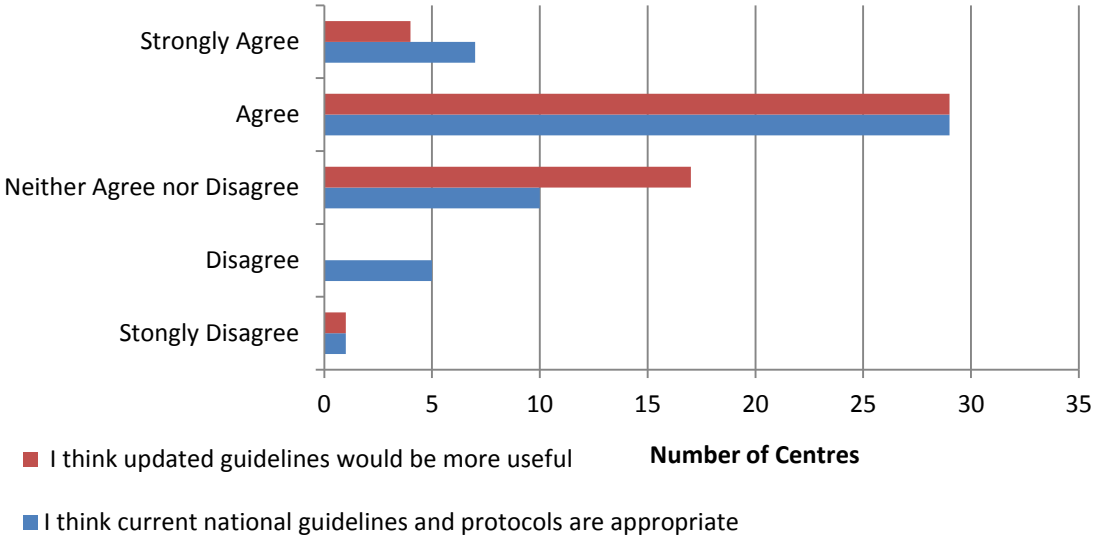

Figure 1. Opinion of current guidelines

When asked if updated, more specific guidelines would be useful two thirds of all centres indicated more updated guidelines are needed.

RCR 2004

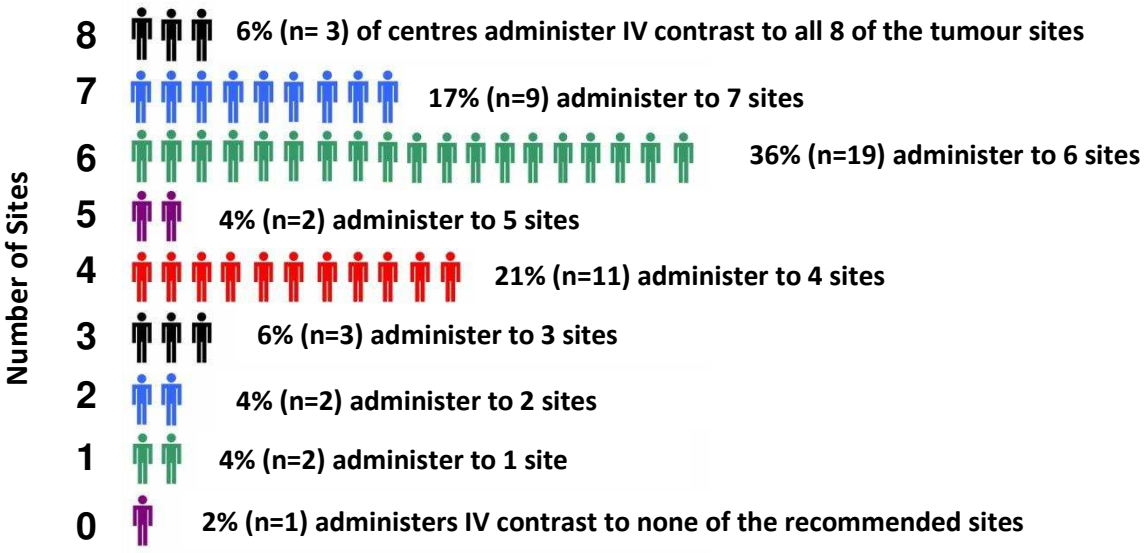

Figure 2: Centres administering IV contrast to the 8 recommended sites RCR 2004[2]

Of the 52 centres that replied, only 6% (n=3) centres administer IV contrast to all 8 recommended tumour sites. The most common sites were lung (94%, n=49), and head and neck nodes (92%, n=48); the least common site was liver.

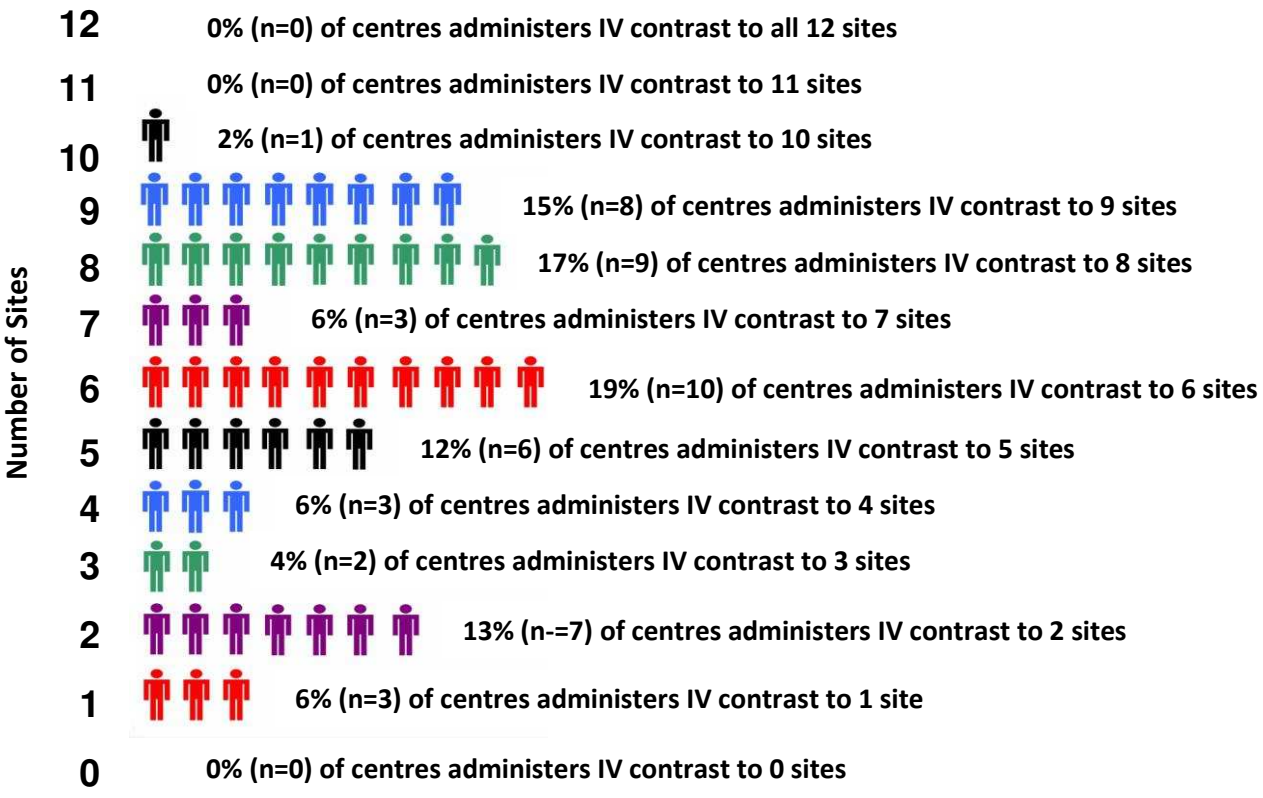

Figure 3: Centres administering IV contrast to the 12 suggested sites RCR 2004[2]

The most common RCR 2004[2] suggested sites that IV contrast is administered for was cervix (85%, n=44), parotid (75% n=39) and rectum (71% n=37); the least common sites was adrenal (12% n=6) and bladder (15% n=8).

There are several sites to which centres routinely deliver IV contrast which are not supported by RCR (2004)[2], including: paranasal sinus (73% n=38), prostate (62% n=32), brain (60% n=31), thyroid (46% n=24), soft tissue sarcoma (29% n=15), spinal cord (12% n=6), testis (6% n=3), anus (4% n=2) and breast (2% n=1).

RCR 2010:

Eighty eight percent (n=46) of centres check kidney function for every patient before administering IV contrast, 8% (n=4) check high risk patients only and 4% (n=2) answered not applicable.

Of the 38 centres using eGFR 17%, (n=9) reported that the formula they used was unknown. The most common known formulas were modified diet in renal diet (MDRD) (15% n=8), Cockcroft Gault (12% n=6) and Wright Formula (12% n=6). The most common eGFR threshold level used was >60 ml/min/1.73m^2 (47%, n=18), although some centres (18%, n=7) used a much lower threshold of >30 ml/min/1.73m^2. Several centres (6%, n=3) stated a change in contrast brand from Omnipaque to Visipaque depending on results of kidney function tests due to a lower risk of nephrotoxicity.

Of the 14 centres using creatinine to calculate kidney function, when asked about creatinine thresholds the majority of centres did not know the level used (43%, n=6), followed by <150µmol/L (29%, n=4) the remaining centres ranged from <120µmol/L to <170µmol/L.

Extravasation advice was provided by the majority of centres, with 85% (n=44) following individual departmental protocols. However, 15% (n=8) had no policy or offered no advice to the patient. Fifty four percent (n=28) ensured the patient is reviewed by a clinician, 42% (n=22) provide an information pack about the reaction or contact details if needed. Treatment options were varied with 48% (n=25) using a cold compress to reduce swelling, 12% (n=6) apply pressure or massage.

Range of Practice:

Over half of the centres (54%, n=28) stated current protocols were based on a mix of RCR guidelines, manufacturers recommendations and diagnostic protocols. Twelve percent (n=6) also stated protocols were adapted based on a range of practices including clinician input, experience and National Institute for Health and Care Excellence (NICE) guidelines.

Contrast, Cannula and Timings:

Flow rate reported was varied, with a wide range of protocols being utilised (range 1-4ml/second) for dynamic pump administration. For brain tumours 17% (n=9) centres hand inject whereas 4% (n=2) drop the flow rate to 1ml/second.

IV contrast volume delivered also varied (range 50ml - 100ml). The majority of centres (38% n=20) delivered 100ml for all patients, whereas 15% (n=8) change volumes depending on patient weight or tumour site. However for enhancing brain tumours, 33% (n=17) of centres use 50ml of contrast. Only 2% (n=1) centres administer more contrast (120mls) for 4DCT. Centres reported contrast enhancement to be sufficient from current protocols always (33%, n=17) or most of the time (67%, n=35).

Advanced techniques:

Bolus tracking where a threshold level of contrast enhancenet must be reached within a region of interest before the scan is acquired was reported by 10% (n=5) and saline chasers used by 6% (n=3) of centres. Only 1 of the 5 centres who use bolus tracking found enhancement to always be sufficient, similarly only 1 of the 3 of the centres using saline chasers found enhancement to always be sufficient.

Fifty four percent (n=28) of centres merge the planning scan with a previous diagnostic scan if contrast enhancement is not sufficient, 25% (n=13) take no action, 21% (n=11) will use PACS images as a reference but will not merge them.

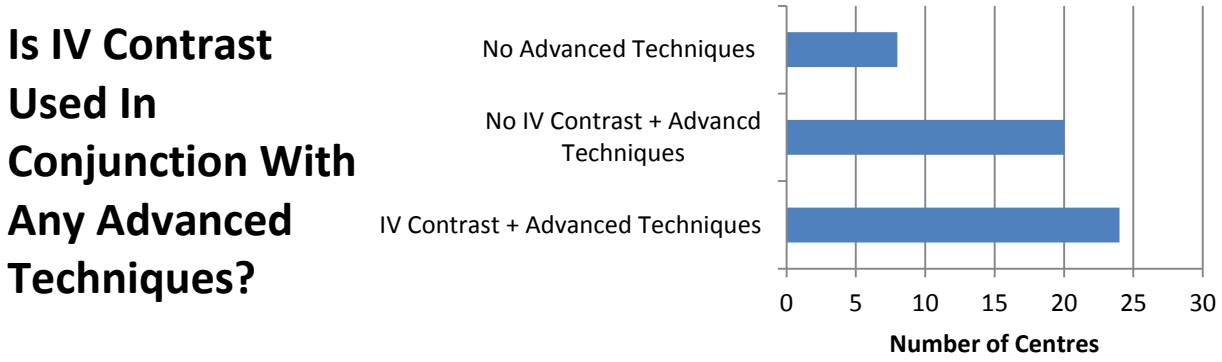

Figure 5. IV contrast in conjunction with advanced techniques

4DCT is used by 46% (n=24) of the centres, however only 35% (n=18) use IV contrast with 4DCT. Of the centres that don't use IV contrast with 4DCT (n=6), most of the patients are being dual scanned, i.e. IV contrast for 3D scan/ volume of interest (VOI) followed by non-contrast 4DCT.

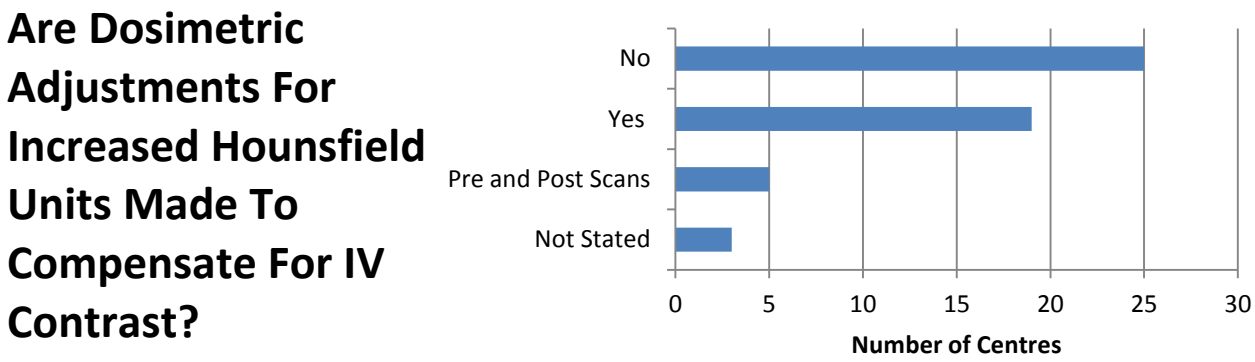

Figure 6. Dosimetric adjustments for increased Hounsfiled units

Digitally reconstructed radiograph (DRR) quality is not an issue in 88% (n=46) centres, the contrast is manually removed or overridden using planning software in the remaining 12% (n=6) centres.

Patient Care and Information:

Ninety six percent (n=50) of centres reported providing post injection advice to patients, the remaining 4% (n=2) state they give no advice. The most frequent time reported that patients are asked to remain in the department following IV contrast injection was 30 minutes (13% n=7).

Hydration advice was varied, the majority of centres (58% n=30) do not quantify fluid increase, instead advising a general increase or to drink 'plenty'.

The length of time that patients are advised to increase their fluid intake for was specified by 19 centres, with 23% (n=12) advising a minimum of 24 hours and 13% (n=7) advising a minimum of 48 hours; the remaining 64% (n=33) of centres did not specify a required minimum time.

Written information is provided by 17% (n=9) centres; whereas 4% (n=2) of centres provide verbal instructions only. Additional information is also provided by a number of centres with 13% (n=7) providing contact details, 8% (n=4) advising going to GP if any problems occur and 13% (n=7) advised to attend A&E if any problems.

Training:

In house training was varied and ranged from several centres (9% n=5) utilising structured Post Graduate Diploma (PGD) and life support training prior to contrast delivery, with one centre only requiring shadowing of diagnostic colleagues as a minimum. Competency requirements were also varied with one centre requiring only 8 supervised cannulations compared to another centre requiring 6 months of supervised practice.

Overall staff felt current training is sufficient (87% n=45), however several additional comments were given stating a wish for more training on practicalities of administering IV contrast, specific information about contrast agents, specific radiotherapy support in relation to IV cannulations and extravasations and reactions.

Discussion

RCR 2004 compliance

The use of IV contrast within RTP CT scans has significantly increased with 98% (n=51) of centres now routinely administering to at least 1 site; compared to 57% (n=33)[5] and 76% (n=38)[4] in previous studies. RCR (2004)[2] recommended tumour sites has also increased with 6% (n=3) of centres now administering to all 8 sites, compared to zero centres as identified in previous studies[4,5]. Full compliance is still relatively poor with over 40% of centres administering to only 5 sites or less, however it is acknowledged that not all centres will routinely treat all tumour sites. Findings are similar with the 12 suggested sites; nearly 60% of centres were found to administer to only 6 or less of the sites. Yet increased frequency is identified in sites such as paranasal sinus, prostate and brain, which were not previously indicated by RCR (2004)[2]; these sites are most likely utilised due to adoption of clinical trial protocols and as a result of individual departmental requirements. Results identified an increased awareness of existing guidelines with only (8%, n=4) stating they were unaware of the content, compared to a previous survey 30% (n=15)[4].

RCR 2010 compliance

The majority of centres (88%, n=46) check eGFR for every patient. The exact risk of contrast-induced nephrotoxicity remains unknown due to insufficient long-term follow up[3]. However, the main risks as identified by RCR (2010)[3] are anaphylaxis, contrast induced nephrotoxicity, nausea, vomiting, urticaria, bronchospasm, laryngeal oedema and hypotension. The risk of a patient developing a severe reaction is 0.4% and risk of developing a very severe reaction 0.004% based on a single centre study (n=298,491) between 2002 -2006[6]. RCR (2010)[3] guidelines identify high-risk patients as those with a history of previous reaction to contrast, asthma, renal problems or diabetes. These risk factors are not necessarily contra-indications; instead they are situations where further assessment should be made; ultimately the choice to use contrast is dependent on benefit-risk ratio.

Of concern is lack of knowledge regarding the formula used to calculate eGFR due to the known discrepancies identified in the literature[7,8,9]. There is currently no national guidance as to which eGFR calculation formula should be used to ensure accurate assessment of kidney function prior to IV contrast delivery. However, results from the literature would indicate the Wright Formula[7] which uses both Jaffé and Enzymatic creatinine assays to be the most accurate, less biased and more applicable to the cancer population when compared against other formulas[8,9]. There is also little consistency of recognised threshold levels when IV contrast should not be delivered, >60 ml/min/1.73m^2 is used by the majority of centres (47%, n=18/38), as recommended by RCR (2010)[3], which states thresholds can be changed with local guidance. Yet, with results as low as >30 ml/min/1.73m^2, caution must be maintained and further research is suggested. Also concerning, 15% (n=8) of centres don't have extravasation policies, despite being a known risk of IV contrast administration; increased compliance should be made a priority to ensure and maintain patient safety.

Range of practice

There was an apparent wide variation in practice identified in the results. Flow rates varied between 1-4mls/second (although 85% (n=44) use flow rates of 1-3mls/second) for routine IV contrast delivery which was comparable to evidence provided by Schwab et al (2009)[10] who identified flow

rates of 2-5ml/second were feasible and found to be safe in delivering IV contrast without an increased risk of extravasation. While patient safety is paramount, enhancement achieved in using IV contrast is also critical in order to justify the risk/benefit ratio, little evidence exists relating to optimal flow rates and the subsequent level of enhancement, suggesting further research is required.

4DCT is used by 46% (n=24) of the centres, however only 35% (n=18) use IV contrast with 4DCT. Of the centres that don't use IV contrast with 4DCT (n=6), most of the patients are being dual scanned. This should be prevented in order to adhere to as low as reasonable practicable (ALARP) principles. Additional research and collaboration with centres with existing 4DCT IV protocols is suggested.

Dosimetric adjustments were made by 36% (n=19) of centres whereas 48% (n=25) make no adjustments, evidence supporting this is varied. Current evidence however suggest there is only minimal impact on dose calculation caused by raised Hounsfield units of IV contrast media, with typical increases of less than 1%[11,12,13]. Significant increases in dose have been observed where beams pass through multiple organs and blood vessels[11], suggesting adjustments should be made based on anatomical tumour sites or on an individual patient basis rather than routinely performed.

Advanced techniques in conjunction with IV contrast delivery were utilised by 46% (n=24) of centres, including 4DCT, saline chasers and bolus tracking. However of those centres using bolus tracking (10%, n=5) only one centre found enhancement to always be sufficient, similarly of the 6% (n=3) using saline chasers, only one centre found enhancement to always be sufficient. This is comparable to results by Dorio et al (2003)[14] who found no benefit in IV contrast enhancement when using saline chasers. However opinions relating to sufficiency of IV contrast enhancement are subjective and may not be truly representative of enhancement outcomes.

It must be noted that the majority of current evidence is based on small single centre studies and therefore further research is suggested to promote standardisation and development of optimal protocols where possible. In order to achieve this standardised assessment,objective measures to compare IV contrast enhancement must be first be defined.

Current guidelines versus current practice

Current guidelines are limited as they only reflect tumour sites and standards of administration; no guidance exists on protocols, training requirements, IV contrast delays, flow rates or administration in conjunction with advanced techniques. It has been identified that even with guidance in place compliance is poor. With the keys results indicating:

- Only 6% (n=3) centres administering to all 8 tumour sites
- Over 70% over centres deliver IV contrast to at least one additional tumour site which isn't recommended by RCR (2004)[2]
- 15% (n=8) of centres not having extravasation policies
- 17% (n=9) of centres reporting eGFR formula used was unknown

These results indicate even for areas where guidance exists, compliance is poor. These areas need to be addressed as a priority to ensure compliance is improved and centres are adhering to recommended evidence based guidance.

Limitations

The main limitation of this study is lack of knowledge of the actual level of IV contrast enhancement achieved using current protocols at individual centres. For the current study centres were only asked how sufficient they feel the enhancement achieved using current protocols is, using a Likert scale response. This is a subjective question and doesn't qualify actual benefit; as generally centres have no other data for comparison. Due to this limitation a full further research study is needed in order to compare several tumour sites multiple times in order to truly measure and quantify enhancement; this was deemed outside the constraints of the current study due to time and resource limitations, but would be of value to assessing sufficiency of imaging quality.

Conclusion

It is clear from the findings that new guidance specific to radiotherapy planning is required covering a wider area of IV practice to ensure optimal protocols are adopted that reflect the current evidence base. This is supported with two thirds of centres agreeing or strongly agreeing when asked if updated guidelines would be useful. Recommendations include:

- Recommended tumour sites should be redefined to reflect current evidence based practice, including tumour sites identified from clinical trials where IV contrast is beneficial in aiding target delineation and identifying organs at risk.
- eGFR and other known risk factors should be routinely assessed for all patients to maintain patient safety and minimise risk of long-term side effects and complications.
- Further research into the most accurate eGFR calculation formula and levels should be undertaken in order to establish a gold standard due to the increased prevalence of IV contrast use.
- Extravasation policies should be mandatory for all centres delivering IV contrast to maintain and protect patient safety.
- Dosimetric adjustments should be made based on anatomical tumour sites or on an individual patient basis rather than routinely performed.
- Dual scanning should be minimised where possible to ensure adherence to as low as reasonably practicable (ALARP) principles.
- Additional research is required to develop objective measures of IV contrast enhancement to allow optimal protocols to be developed.

References

1. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology 2010; 256: 32–61.

2. Royal College of Radiologists. Imaging for Oncology: Collaboration between Clinical Radiologists and Clinical Oncologists in Diagnosis, Staging and Radiotherapy Planning. 2004. London: The Royal College of Radiologists.

3. Royal college of Radiologists. Standards for intravascular contrast agent administration to adult patients. Second edition. 2010. London: The Royal College of Radiologists .

4. Kim S, Russell W, Price P, Saleem A. Suboptimal use of intravenous contrast during radiotherapy planning in the UK. Br J Radiol 2008; 81(972): 963-9.

5. Jefferies S, Taylor A, Reznek R. Radiotherapy Planning Working Party. Results of a national survey of radiotherapy planning and delivery in the UK in 2007. Clin Oncol (R Coll Radiol) 2009; 21(3): 204–17.

6. Hunt CH, Hartman RP, Hesley GK. Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: retrospective review of 456,930 doses. AM J Roentgenol. 2009; 193: 1124-1127.

7. Wright JG, Boddy AV, Highley M, Fenwick J, Calvert AHl. Estimation of glomerular filtration rate in cancer patients. Br J Cancer 2001; 84: *452*–459.

8. Marx GM, Steer CB, Galani E, et al. Evaluation of the Cockroft and Gault, Jelliffe and Wright formulae in the estimation of renal function in elderly patients. Ann Oncol 2004; 15: 291-295.

9. Barraclough LH, Field C, Wieringa G, Swindell R, Livsey JE, Davidson SE. Estimation of renal function-what is appropriate in cancer patients. Clin Oncol (R Coll Radiol) 2008; 20**:** 721–726.

10. Schwab SA, Uder M, Anders K et al. Peripheral intravenous power injection of iodinated contrast media through 22G and 20G cannulas: can high flow rates be achieved safely? A clinical feasibility study. Acad Radiol 2009; 16(12): 1502-8.

11. Shibamoto Y, Naruse A, Fukuma H, Ayakawa S, Sugie C, Tomita N. Influence of contrast materials on dose calculation in radiotherapy planning using computed tomography for tumors at various anatomical regions: a prospective study. Radiother Oncol. 2007; 84: 52–55.

12. Choi Y, Kim JK, Lee HS et al. Influence of intravenous contrast agent on dose calculations of intensity modulated radiation therapy plans for head and neck cancer. Radiother Oncol. 2006; 81: 158–162.

13. Xiao J, Zhang H, Gong Y et al. Feasibility of using intravenous contrast-enhanced computed tomography (CT) scans in lung cancer treatment planning. Radiother Oncol. 2010; 96: 73–77.

14. Dorio PJ, Lee FT, Henseler KP et al. Using a saline chaser to decrease contrast media in abdominal CT. AM J Roentgenol. 2003; 180: 929-934.