INTRODUCTION

Soft tissue sarcomas (STS) are a rare, heterogeneous tumour group with an incidence of 4–5/100,000 people in Europe.1 Radical treatment involves a combination of radiotherapy and surgery for intermediate or high risk disease.2–4 Combined treatment has been shown to minimize local recurrence whilst maintaining function and moderating long term toxicity.5–7

Tumour volume contouring is undertaken on contrast-enhanced CT. However, CT has poor soft tissue contrast making contouring of STS difficult, as the extent of disease is poorly visualized. Indeed, a study by Wang et al demonstrated interobserver variation amongst radiation oncologists when contouring the clinical target volume of STS on pre-operative CT scans alone.5 Difficulty in contouring, including deviations from protocol and variation in contouring tumour volumes, is an important factor in treatment failure.5,10 Consensus amongst oncologists when contouring is important for quality assurance in radiotherapy treatment planning, with variation amongst oncologists often cited as the weakest link.

MRI promises improved soft tissue contrast, and offers both anatomical and functional imaging.11 There is a growing interest in incorporating MRI into the radiotherapy planning pathway for a number of treatment sites, including STS.12 The use of MRI has grown in STS, e.g., in diagnosis, staging and follow-up.13 It is recommended that CT and MR images are co-registered for radiotherapy planning.
although this is not feasible in all centres. Furthermore, the use of MRI in STS radiotherapy planning has not been extensively studied. The major benefit of MRI for STS is that improved visualization of the disease will improve confidence in tumour volume contouring, reducing variation between radiation oncologists. Additionally, better visualization should result in smaller tumour volumes because the full extent of the patient’s disease can be identified. Ultimately, improved accuracy in tumour contouring alongside advanced radiotherapy techniques may allow for dose escalation and improved local disease control.\textsuperscript{16,17}

Improved accuracy may also minimize normal tissue toxicity to nearby critical structures, such as the brachial plexus in an upper limb STS. This may reduce acute and chronic radiotherapy related toxicities, preserving long-term function for patients.\textsuperscript{13}

No published studies have directly compared CT only contouring to MRI only contouring for STS in the same patients. Therefore, the direct benefit of MRI in contouring STS has yet to be fully demonstrated. This work aims to directly compare, for the first time, inter- and intraobserver variation between oncologists contouring tumour volumes for STS on CT and MRI.

**METHODS AND MATERIALS**

Eight patients diagnosed with STS and treated with neoadjuvant radiotherapy prior to definitive surgery were selected from a previous research study. This previous study had received approval from the local ethics committee, and its primary objective was to correlate the histological response of soft tissue sarcoma after pre-operative radiotherapy with pre-treatment MRI parameters of DCE (dynamic contrast enhanced) MRI and DWI (diffusion-weighted imaging) MRI. Patient demographics are included in Table 1. All patients underwent pre-treatment radiotherapy planning contrast-enhanced CT and MRI in the supine position, at less than 1 week apart. CT and MRI protocols were the same for all patients. CT slices were 3 mm thick. For MRI, axial $T_2$ weighted turbo spin echo images were acquired and used for contouring in this study. The imaging parameters were: repetition time 3790 ms; echo time 99 ms; Matrix $448 \times 448 \times 29$; Slice thickness 10 mm; ETL 13; field of view $400 \times 400$ mm.

For interobserver analysis, four radiation oncologists trained in contouring STS independently contoured the gross tumour volume (GTV) for each patient on both imaging modalities using in-house contouring software.\textsuperscript{18} Contouring was performed in the axial plane using a soft-tissue level and window, each oncologist optimizing this to visualize the disease. CT and MRI scans were fully anonymized and oncologists were blinded to which CT and MRI belonged to the same patient.

Interpatient analysis was performed by first creating a median contour volume from the four oncologist contours. This was done as a whole volume and acted as the truth contour. All individual oncologist contours were compared against this median volume, calculating a signed mean distance to agreement (mDTA).\textsuperscript{19} This approach looks for the closest distance between each point on the contour and the truth contour. The mDTA provides a good comparison of each oncologists contour against the truth volume across the whole volume. In addition to the mDTA, the standard deviation (SD) of the DTA between each oncologist and the truth contour was calculated. This indicates the level of agreement around the whole contour, with lower values showing better all-round agreement. Finally, the dice similarity coefficient (DSC) was calculated. This is the ratio of twice the volume of the union of the truth and test contour and the total volume of the truth and test volumes. DSC is summarized by the equation: $DSC(A,B)=2(A \cap B)/(A + B)$ where $A$ and $B$ are the truth and test contour volumes respectively, and $\cap$ is the volume of the intersection of the two contours. A value of 1 indicates perfect overlap and 0 no overlap.\textsuperscript{19–21} The volume of each contour, on CT and MRI, was also collected.

**Table 1. Summary of patient demographics**

| Patient number | Gender | Age at diagnosis | Tumour location | Histology | FNCLCC grade | Maximum diameter (cm) |
|----------------|--------|------------------|----------------|-----------|--------------|----------------------|
| 1              | Male   | 72               | Medial aspect left upper arm | Myxofibrosarcoma | 2           | 9.0                  |
| 2              | Male   | 56               | Left lateral thigh | Myxoid liposarcoma | 2           | 6.0                  |
| 3              | Male   | 27               | Medial aspect right knee | Extraskeletal myxoid chondrosarcoma | 3           | 7.3                  |
| 4              | Male   | 29               | Anterior aspect right lower leg | Spindle cell carcinoma | 3           | 5.1                  |
| 5              | Male   | 41               | Anterior aspect left lower leg | Myxoinflammatory fibroblastic sarcoma | 1           | 2.7                  |
| 6              | Male   | 62               | Medial aspect right forearm | Myxofibrosarcoma | 3           | 5.1                  |
| 7              | Male   | 24               | Lateral aspect left knee | Synovial sarcoma NOS | 3           | 8.4                  |
| 8              | Male   | 73               | Lateral aspect right anterior chest wall | Undifferentiated spindle cell sarcoma | 3           | 5.2                  |

FNCLCC, Fédération nationale des centres de lutte contre le cancer; NOS, Not otherwise specified.
RESULTS

Figure 1 illustrates contouring for two representative patients, highlighting the improved soft tissue contrast of the STS on MRI compared with CT. The contours of the four oncologists are shown on both CT images (Figure 1A and B) and MRI images (Figure 1C and D), illustrating the benefit seen with MRI in reducing interobserver variation. All GTV delineations were returned except for one oncologist who did not contour the CT or MRI for Patient 3.

The results for interobserver variation showed significant improvement in using MRI for delineation. Figure 2 shows box and whisker plots for mDTA, SD of DTA, DSC and volumes. Table 2 summarizes these results, presenting the mean values across all oncologists and the results of the pairwise Student’s t-test. The mDTA between CT and MRI based contours did not show a statistically significant improvement (p = 0.3) However,
the SD of the DTA did show a statistically significant improvement on using MRI ($p = 0.04$). Figure 2b illustrates an improvement for six of the eight patients with the maximum SD on CT of 5.5 vs 4.6 mm on MRI. This indicates that although overall mDTA is not improved on MRI, the oncologists are contouring more consistently. Similarly to the mDTA, the DSC did now show a statistically significant difference in moving to MRI based delineation.

Finally, the mean volume contoured on CT was 88.7 cm$^3$ compared to 67.3 cm$^3$ on MRI ($p = 0.008$). Contouring on MRI resulted in a lower volume for every patient, with Patient 1 and Patient 7 showing a marked reduction in volume on MRI.

Intraobserver results are summarized in Table 3 and show no statistically significant improvement in using MRI. The SD of DTA and DSC showed a modest improvement but these were not significant. The volumes delineated by each oncologist showed slightly better consistency on MRI than CT. The ratio of volumes (median across all oncologists) delineated at each time point was 0.97 for CT and 0.99 for MRI. However, this was not a statistically significant improvement ($p = 0.7$).

**DISCUSSION**

To our knowledge, this is the first study to directly compare inter- and intraobserver variation when contouring tumour volumes for STS on CT only and MRI only. Each patient was imaged with CT for radiotherapy planning and with anatomical $T_2$ weighted MRI acquired as part of a research study. Our results showed that oncologists uniformly contoured smaller tumour volumes using MRI vs CT, by 21.4 cm$^3$ across all patients ($p = 0.008$). The improved soft tissue contrast provided by MRI allows the disease to be better visualized. This allows greater confidence in contouring with oncologists better able to minimize the volume they wish to treat. This reduction in volume has the potential to deliver reduced normal tissue toxicities for this group of patients, potentially leading to improved function.

Other groups have previously aimed to quantify inter- and intraobserver variation in STS contouring using CT or MRI. Wang et al demonstrated interobserver variation amongst 10 radiation oncologists when contouring an upper limb sarcoma on CT. Briefly, oncologist agreement was assessed by calculating apparent volume overlap, and then correcting for agreement by chance using generalized $k$ statistics. Oncologists had MRI images available, but co-registration with CT images was not possible for all patients as MRI scans were not performed in the treatment position. A result of $k = 0.77$ for upper limb clinical target volume contouring indicated less than perfect agreement according to Londis and Koch criteria. However, they did not comment on intraobserver variation. Baldini et al similarly used $k$ statistics to demonstrate a high agreement between 11 radiation oncologists when contouring the GTV for two retroperitoneal STS patients using CT images. The Roberge study used Boolean analysis to assess the degree of volume overlap as a measure of variation amongst five clinicians when contouring STS on MRI images, with a median tumour volume overlap of 79 and 93% for inter- and intraobserver contours respectively. Sargos et al, distributed co-registered CT and MRI images to six radiation oncologists, demonstrating substantial agreement by $k$ statistics in a single pre-operative patient. However, the above studies did not directly compare inter- and intraobserver variation between CT and MRI.

Other groups have compared inter- and intraobserver variation amongst CT and MRI for other tumour sites, with mixed results. Rasch et al observed reduced interobserver variation with MRI when contouring head and neck tumours. Al-Hammadi et al reported improved generalized conformity index and accuracy index with MRI vs CT when contouring the postoperative breast cancer lumpectomy cavity for radiotherapy planning, indicating reduced interobserver variation. However, this study had low numbers of patients and oncologists. Karli et al found no difference in interobserver variation between MRI and PET-CT for non-small-cell lung carcinoma radiotherapy planning, when using a bidirectional local distance measure to compare individual clinicians’ contours with a median contour. Barkati et al observed a higher DSC using CT vs MRI for prostate radiotherapy planning, indicating increased interobserver variation with MRI.

Several other groups have looked at the value of adding MRI images to CT images in reducing interobserver variation vs CT alone. Villeirs reported that the addition of MRI to CT reduced both the contoured volume and the interobserver variation for prostate radiotherapy planning vs CT alone. The addition of MRI to CT has been observed to increase the concordance index when contouring high grade gliomas, indicating reduced interobserver variation. CT and MRI image registration has been similarly shown to reduce interobserver variation in other central nervous system tumours.

Interestingly, the mean DTA was not significantly different between MRI and CT ($p = 0.3$) in this study. However, the SD of the DTA was significantly smaller for MRI ($p = 0.04$). This
suggests more consistent contouring of the tumour around the whole contour between the clinicians. Visual inspection highlighted better agreement in the superior–inferior extent of the disease. The extent of disease along the muscle is difficult to interpret on CT and this may be the great benefit of MRI. The better agreement on MRI in these areas may be the reason for the improvement in the SD of the DTA between oncologists.

No difference in intraobserver variation was found between MRI and CT. This result was surprising given the potential advantages in improved soft tissue delineation that MRI offers, and could partially be due to a small study sample and learned experience from the earlier contouring. Alternatively, the oncologists involved in the study are highly experienced in contouring with CT images, but less so with MRI. Further training and experience using MRI may allow the full potential of this modality to be realized. It may prove advantageous to repeat this study in the future once a higher level of experience has been reached.

There were several limitations to this study. It was conducted at a single centre, and due to the rare nature of STS only four trained oncologists were available for contouring, with only three performing the intraobserver delineation exercise. In the Wang et al and Baldini et al studies, 10 and 11 clinicians respectively returned contours. Similarly, we only had 8 patients, limited by the availability of suitable patients with both CT and MRI available, whereas the Roberge et al study had 15. A limitation for all studies looking at inter- and intraobserver contouring variation is that the results of individual clinicians are compared against other clinicians and the mean or median contour. There is a lack of a “Gold-Standard” for comparison of results. \( T_2 \) weighted images allow visualization of peritumoral oedema, and the necessary inclusion of this oedema may have led to oncologists contouring larger tumour volumes. Indeed, work by White et al demonstrated that peritumoural signal changes seen on \( T_2 \) weighted MRI scans ranged from 0 to 5.3 cm (mean 1.1 cm). This could also account for increased interobserver variation amongst oncologists with MRI due to different interpretations of tumour tissue versus oedema. MRI has the capability to reflect a range of tissue properties. For example, gradient echo imaging may be used for detection of haemorrhage, and \( T_2 \) weighted fat suppressed sequences may differentiate haemorrhage from fat. Biopsiable solid tumour can be differentiated from necrotic tissue with gadolinium-enhanced sequences. Gadolinium may also allow for visualization of cystic components of tumours. Vascular structures are more easily visualized with MRI vs CT.

There are also limitations to the analyses. DSC is driven by volume, and large volume contours can have a higher DSC but display poor agreement. Conversely, smaller volume contours may have good agreement but poor DSC. This is illustrated in Figure 2 where patient five has the smallest volume (2d) and the worst DSC (2c) despite showing a reasonable mDTA (2a). DTA may be a better representation of consistency and agreement amongst oncologists. However, by generalizing values to a mean value across the entire contour, small local benefits may be hidden.

There are several challenges to an MRI-based radiotherapy planning system. Many radiotherapy departments lack a dedicated MRI machine and so would have to compete for timeslots with other departments and services for MRI planning scans. Thus, departments may not have access to MRI for all patients, and there are inherent challenges with co-registration of CT and MRI images. MRI scanning is more costly than CT and scanning times are longer. This may be particularly problematic for comorbid patients who struggle to lie flat for extended periods. However, immobilization devices are being made MRI safe. It may be difficult to scan patients in a treatment position in the confines of the MRI bore whilst maintaining image quality, although larger 70 cm bore systems are becoming available at 1.5 and 3.0 T. Additional receiver coil configurations have been developed, as well as devices which raise existing receiver coils above the patient to prevent coil weight disturbing patient anatomy. Such bridge coils are already becoming common in radiotherapy scanning. There is potential for large errors to be introduced into the planning process due to geometric distortion in MRI images. The degree of distortion depends on many factors including scanner manufacturer, field strength, main magnetic field inhomogeneity, gradient non-linearity, sequence type, choice of sequence parameters such as bandwidth, and the distance of the region of interest from isocentre. For an individual scanner, rigorous quality assurance should be undertaken to ensure that geometric distortion is minimized. Manufacturer-supplied distortion correction algorithms are commonly applied to MR images, and these have been shown to reduce distortion to less than 2 mm. This highlights the importance of rigorous QA and strict adherence to standard protocols when acquiring MR images for RT planning. Additionally, dose calculations may be difficult in the absence of Hounsfield units and density overrides or corrections applied. However, progress is being made in this field, and Philips have a commercial product for planning prostate radiotherapy using MRI. The factors above will need to be considered once clinical benefit has been demonstrated.

Other groups have looked at ways of reducing contouring variation amongst oncologists. Bowden et al showed that providing oncologists with a clear protocol results in a reduction in interobserver variation in lung tumour contouring. However, other work has shown that this effect may be reduced with more experienced oncologists. Other suggestions include involving two oncologists in the contouring of a tumour, and Hollingdale et al recently completed a prospective study highlighting the feasibility of oncologists working with radiologists to increase accuracy and confidence in tumour contours. The above work was carried out for CT imaging but similar principles could be applied to MRI. It was beyond the scope of our study to comment on the effect of the level of training. However, it is likely that comprehensive training would be needed if MRI were to be introduced as standard for radiotherapy planning in STS. Further work could involve a greater number of oncologists and patients, perhaps across several centres. It would be interesting to clarify the reason for increased variation with some images, the effects of training grade, or whether histological subtype is an important factor, and we could also look at the effect of different...
MRI sequences. For example, the addition of DWI could allow better visualization of tumour vs healthy tissue, and lead to smaller tumour contours.

In conclusion, we aimed to compare inter- and intraobserver variation amongst radiation oncologists when contouring tumour volumes for STS on CT only vs MRI only for the first time. We did not observe a significant difference in intraobserver variation between CT and MRI. However, we showed reduced interobserver variation using MRI, with oncologists delineating smaller volumes and more consistent contours. In radiotherapy treatment planning, accurate margins are important in allowing maximum dose to be given to the area of disease and to minimise dose given to normal tissue. As imaging technology advances, accurate contouring continues to be limited by oncologist interpretation of images. Improving the reliability and consistency of tumour contouring is needed for improved quality assurance. With further experience and training the use of MRI in STS may reduce variation between oncologists and contribute to improved local control and reduced treatment toxicities.

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REFERENCES
1. Gatta G, van der Zwan JM, Casali PG, Siesling S, Dei Tos AP, Kunkler I, et al. Rare cancers are not so rare: the rare cancer burden in Europe. *Eur J Cancer* 2011; 47: 2493–511.Available from [Internet]. doi: https://doi.org/10.1016/j.ejca.2011.08.008
2. O’Sullivan B, Ward I, Catton C. Recent advances in radiotherapy for soft-tissue sarcoma. *Carr Oncol Rep* 2003; 5: 274–81.Available from [Internet]. doi: https://doi.org/10.1006/s11912-003-0066-y
3. Strander H, Turesson I, Cavallin-Stahl E. A systematic overview of radiation therapy effects in soft tissue sarcomas. *Acta Oncol* 2003; 42(5–6): 516–31.Available from [Internet]. doi: https://doi.org/10.1080/02841860310014732
4. Maples WJ, Buskirk SJ. Multimodality treatment of upper extremity bone and soft tissue sarcomas. *Hand Clinics* 2004; 20: 221–5.Available from [Internet]. doi: https://doi.org/10.1016/j.hcl.2004.03.021
5. Rosenbaum SA, Tepper J, GLATSTEIN ELL, Costa J, Baker A, Brennam M, et al. The treatment of soft-tissue sarcomas of the extremities. *Annals of Surgery* 1982; 196: 305–15.Available from [Internet]. doi: https://doi.org/10.1097/00000658-198209000-00009
6. Yang JC, Chang AE, Baker AR, Sindelar WF, Danforth DN, Topalian SL, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. *JCO* 1998; 16: 197–203.Available from [Internet]. doi: https://doi.org/10.1097/00005656-199802000-00009
7. Koshy M, Rich SE, Mohiuddin MM. Improved survival with radiation therapy in high-grade soft tissue sarcomas of the extremities: a SEER analysis. *International Journal of Radiation Oncology*Biology*Physics* 2010; 77: 203–9.Available from. doi: https://doi.org/10.1016/j.ijrobp.2009.04.051
8. Wang D, Bosch W, Kirsch DG, Al Lozi R, El Naqa I, Roberge D, et al. Variation in the gross tumor volume and clinical target volume for preoperative radiotherapy of primary large high-grade soft tissue sarcoma of the extremity among RTOG sarcoma radiation oncologists. *Int J Radiat Oncol Biol Phys* 2011; 81: e75–80.Available from. doi: https://doi.org/10.1016/j.ijrobp.2010.11.033
9. Peters LJ, O’Sullivan B, Giralt J, Fitzgerald TJ, Trotti A, Bernier J, et al. Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: results from TROG 02.02. *JCO* 2010; 28: 2996–3001.Available from. doi: https://doi.org/10.1200/JCO.2009.27.4498
10. Ohri N, Shen X, Dicker AP, Doyle LA, Harrison AS, Showalter TN. Radiotherapy protocol deviations and clinical outcomes: a meta-analysis of cooperative Group clinical trials. *J Natl Cancer Inst* 2013; 105: 387–93.Available from [Internet]. doi: https://doi.org/10.1093/jnci/djt001
11. Krasndorf MJ, Murphrey MD. Radiologic evaluation of soft-tissue masses: a current perspective. *AJR Am J Roentgenol* 2000; 175: 575–87.Available from [Internet]. doi: https://doi.org/10.2214/ajr.175.3.1750575
12. Owrami AM, Greer PB, Glide-Hurst CK. MRI-only treatment planning: benefits and challenges. *Phys Med Biol* 2018; Available from [Internet].
13. Dangoor A, Seddon B, Gerrand C, Grimer R, Whelan J, Judson I. UK guidelines for the management of soft tissue sarcomas: why, when, and where? *International Journal of Radiation Oncology*Biology*Physics* 2012; 84: 572–80.Available from [Internet]. doi: https://doi.org/10.1016/j.ijrobp.2012.01.062
14. Baldini EH, Wang D, Haas RLM, Catton CN, Indelicato DJ, Kirsch DG, et al. Treatment guidelines for preoperative radiation therapy for retroperitoneal sarcoma: preliminary consensus of an international expert panel. *International Journal of Radiation Oncology*Biology*Physics* 2015; 92: 602–12.Available from [Internet]. doi: https://doi.org/10.1016/j.ijrobp.2015.02.013
15. Alektiar KM, Brennan ME, Healey JH, Singer S. Impact of intensity-modulated radiation therapy on local control in primary soft-tissue sarcoma of the extremity. *JCO* 2008; 26: 3440–4.Available from [Internet]. doi: https://doi.org/10.1200/JCO.2008.16.6249
16. Folkert MR, Singer S, Brennan MF, Kuk D, Qin L-X, Kobayashi WK, et al. Comparison of local recurrence with conventional and intensity-modulated radiation therapy for primary soft-tissue sarcomas of the extremity. *JCO* 2014; 32: 3236–41.Available from [Internet]. doi: https://doi.org/10.1200/JCO.2013.33.9452
17. Wolthaus JWH, van Herk M, Muller SH, Belderbos JSA, Lebesque JV, de Bois JA, Herk Mvan, Bois JAd, et al. Fusion of respiration-correlated PET and CT scans: correlated lung tumour motion in anatomical and functional scans. *Phys Med Biol* 2005; 50: 1569–83. doi: https://doi.org/10.1088/0031-9155/50/7/017
18. Beasley WJ, McWilliam A, Atkenhead A, Mackay RI, Rowbottom CG. The suitability of common metrics for assessing parotid and larynx auto-segmentation accuracy. *J Appl Clin Med Phys* 2016; 17: 41–9. doi: https://doi.org/10.1200/jacmp.1712.5889
19. Dice LR. Measures of the amount of ecologic association between species. *Ecology* 1945;
26. 297–302. doi: https://doi.org/10.2307/1932409

21. Zou KH, Warfield SK, Bharatha A, Temppany CMC, Kaus MR, Haker SJ, et al. Statistical validation of image segmentation quality based on a spatial overlap index. *Acad Radiol* 2004; 11: 178–89Available from[Internet]. doi: https://doi.org/10.1016/S1076-6332(03)00671-8

22. Roberge D, Skamene T, Turcotte RE, Powell T, Saran N, Freeman C. Inter- and intra-observer variation in soft-tissue sarcoma target definition. *Cancer/Radiothérapie* 2011; 15: 421–5Available from. doi: https://doi.org/10.1016/j.canrad.2011.03.006

23. Baldini EH, Abrams RA, Bosch W, Roberge D, Haas RLM, Catton CN, et al. Retropertitoneal sarcoma target volume and organ at risk contour delineation agreement among NRG sarcoma radiation oncologists. *International Journal of Radiation Oncology*Biology*Physics* 2015; 92: 1053–9Available from[Internet]. doi: https://doi.org/10.1016/j.ijrobp.2014.03.035

24. Sargos P, Charleux T, Haas RL, Michot A, Llacer C, Mouroe-Zabotto L, et al. Pre- and postoperative radiotherapy for extremity soft tissue sarcoma: evaluation of inter-observer target volume contouring variability among French Sarcoma group radiation oncologists. *Cancer/Radiothérapie* 2018; 22: 131–9Available from[Internet]. doi: https://doi.org/10.1016/j.canrad.2017.09.004

25. Rasch C, Keus R, Pameijer FA, Koops W, de Ru V, Muller S, et al. The potential impact of CT-MRI matching on tumor volume delineation in advanced head and neck cancer. *International Journal of Radiation Oncology*Biology*Physics* 1997; 39: 841–8Available from[Internet]. doi: https://doi.org/10.1016/S0360-3016(97)00465-3

26. Al-Hammadi N, Carparotti P, Divakar S, Riyas M, Chandramouli SH, Hammoud R, et al. MRI reduces variation of contouring for boost clinical target volume in breast cancer patients without surgical clips in the tumour bed. *Radiol Oncol* 2017; 51: 160–8Available from[Internet]. doi: https://doi.org/10.1515/raon-2017-0014

27. Karki K, Saraiya S, Hugo GD, Mukhopadhyay N, Jan N, Schuster J, et al. Variabilities of magnetic resonance Imaging-, computed Tomography-, and positron emission Tomography–Computed Tomography–Based tumor and lymph node delineations for lung cancer radiation therapy planning. *International Journal of Radiation Oncology*Biology*Physics* 2017; 99: 80–9Available from. doi: https://doi.org/10.1016/j.ijrobp.2017.05.002

28. Barkati M, Simard D, Taussky D, Delouya G. Magnetic resonance imaging for prostate bed radiotherapy planning: an inter- and intra-observer variability study. *J Med Imaging Radiat Oncol* 2016; 60: 255–9Available from[Internet]. doi: https://doi.org/10.1111/1754-9485.12416

29. Villeirs GM, Van Vaerenbergh K, Vakaet L, Brel S, Claus F, De Neve WJ, et al. Interobserver delineation variation using CT versus combined CT + MRI in intensity-modulated radiotherapy for prostate cancer. *Strahlenther Onkol* 2005; 181: 424–30Available from[Internet]. doi: https://doi.org/10.1007/s00066-005-1383-x

30. Cattaneo GM, Reni M, Rizzo G, Castellone P, Ceresoli GL, Cozzarin C, et al. Target delineation in post-operative radiotherapy of brain gliomas: interobserver variability and impact of image registration of MR(pre-operative) images on treatment planning CT scans. *Radiother Oncol* 2005; 75: 217–23Available from[Internet]. doi: https://doi.org/10.1016/j.radonc.2005.03.012

31. Aoyama H, Shirato H, Nishioka T, Hashimoto S, Tsuchiya K, Kages K, et al. Magnetic resonance imaging system for three-dimensional conformal radiotherapy and its impact on gross tumor volume delineation of central nervous system tumors. *International Journal of Radiation Oncology*Biology*Physics* 2001; 50: 821–7Available from[Internet]. doi: https://doi.org/10.1016/S0360-3016(01)01598-X

32. White LM, Wunder JS, Bell RS, O’Sullivan W, de Ru V, Muller S, et al. The potential impact of CT-MRI matching on tumor volume delineation in advanced head and neck cancer. *International Journal of Radiation Oncology*Biology*Physics* 1997; 39: 841–8Available from[Internet]. doi: https://doi.org/10.1016/S0360-3016(97)00465-3

33. Al-Hammadi N, Carparotti P, Divakar S, Rtyas M, Chandramouli SH, Hammoud R, et al. MRI reduces variation of contouring for boost clinical target volume in breast cancer patients without surgical clips in the tumour bed. *Radiol Oncol* 2017; 51: 160–8Available from[Internet]. doi: https://doi.org/10.1515/raon-2017-0014

34. Varo K, Saraiya S, Hugo GD, Mukhopadhyay N, Jan N, Schuster J, et al. Variabilities of magnetic resonance Imaging-, computed Tomography-, and positron emission Tomography–Computed Tomography–Based tumor and lymph node delineations for lung cancer radiation therapy planning. *International Journal of Radiation Oncology*Biology*Physics* 2017; 99: 80–9Available from. doi: https://doi.org/10.1016/j.ijrobp.2017.05.002

35. Barkati M, Simard D, Taussky D, Delouya G. Magnetic resonance imaging for prostate bed radiotherapy planning: an inter- and intra-observer variability study. *J Med Imaging Radiat Oncol* 2016; 60: 255–9Available from[Internet]. doi: https://doi.org/10.1111/1754-9485.12416

36. Villeirs GM, Van Vaerenbergh K, Vakaet L, Brel S, Claus F, De Neve WJ, et al. Interobserver delineation variation using CT versus combined CT + MRI in intensity-modulated radiotherapy for prostate cancer. *Strahlenther Onkol* 2005; 181: 424–30Available from[Internet]. doi: https://doi.org/10.1007/s00066-005-1383-x

37. Cattaneo GM, Reni M, Rizzo G, Castellone P, Ceresoli GL, Cozzarin C, et al. Target delineation in post-operative radiotherapy of brain gliomas: interobserver variability and impact of image registration of MR(pre-operative) images on treatment planning CT scans. *Radiother Oncol* 2005; 75: 217–23Available from[Internet]. doi: https://doi.org/10.1016/j.radonc.2005.03.012

38. Aoyama H, Shirato H, Nishioka T, Hashimoto S, Tsuchiya K, Kages K, et al. Magnetic resonance imaging system for three-dimensional conformal radiotherapy and its impact on gross tumor volume delineation of central nervous system tumors. *International Journal of Radiation Oncology*Biology*Physics* 2001; 50: 821–7Available from[Internet]. doi: https://doi.org/10.1016/S0360-3016(01)01598-X

39. White LM, Wunder JS, Bell RS, O’Sullivan W, de Ru V, Muller S, et al. The potential impact of CT-MRI matching on tumor volume delineation in advanced head and neck cancer. *International Journal of Radiation Oncology*Biology*Physics* 1997; 39: 841–8Available from[Internet]. doi: https://doi.org/10.1016/S0360-3016(97)00465-3

40. Dewas S, Vautravers-Dewas C, Blanchard P, Pointreau Y, Denis F, Lacroix E, et al. Variabilité inter-radiothérapeutes de la délimitation tumorale en oncologie thoracique : exemples d’intercomparaison de délimitations et impact de la formation. *Cancer/Radiothérapie* 2010; 14: 103–10Available from. doi: https://doi.org/10.1016/j.canrad.2009.11.002

41. Hollingdale AE, Roches TW, Curtin J, Martin WMC, Horan G, Barrett A. Multidisciplinary collaborative gross tumour volume definition for lung cancer radiotherapy: a prospective study. *Cancer Imaging* 2011; 11: 202–8Available from[Internet]. doi: https://doi.org/10.1108/1470-7350.2011.0024