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Original article

Inter-observer agreement in GTV delineation of bone metastases on CT and impact of MR imaging: A multicenter study

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ABSTRACT

Background and purpose: The use of Stereotactic Body Radiotherapy (SBRT) for bone metastases is increasing rapidly. Therefore, knowledge of the inter-observer differences in tumor volume delineation is essential to guarantee precise dose delivery. The aim of this study is to compare inter-observer agreement in bone metastases delineated on different imaging modalities.

Material and methods: Twenty consecutive patients with bone metastases treated with SBRT were selected. All patients received CT and MR imaging in treatment position prior to SBRT. Five observers from three institutions independently delineated gross tumor volume (GTV) on CT alone, CT with co-registered MRI and MRI alone. Four contours per imaging modality per patient were available, as one set of contours was shared by 2 observers. Inter-observer agreement, expressed in generalized conformity index [CIgen], volumes of contours and contours center of mass (COM) were calculated per patient and imaging modality.

Results: Mean GTV delineated on MR ($45.9 \pm 52.0\ cm^3$) was significantly larger compared to CT–MR ($40.2 \pm 49.4\ cm^3$) and CT ($34.8 \pm 41.8\ cm^3$). A considerable variation in CIgen was found on CT (mean 0.46, range 0.15–0.75) and CT–MRI (mean 0.54, range 0.17–0.71). The highest agreement was found on MRI (mean 0.56, range 0.20–0.77). The largest variations of COM were found in anterior–posterior direction for all imaging modalities.

Conclusions: Large inter-observer variation in GTV delineation exists for CT, CT–MRI and MRI. MRI-based GTV delineation resulted in larger volumes and highest consistency between observers.

Bone metastases are a common manifestation of cancer and pain is the most prevalent symptom [1]. Pain has a major influence on quality of life [2]. Conventional radiotherapy is the cornerstone in the management of bone metastases, but the use of Stereotactic Body Radiotherapy (SBRT) is increasing rapidly [3]. Conventional radiotherapy is effective in achieving pain relieve in 60% of the patients with bone metastases, but unfortunately up to 40% of the patients do not achieve sustainable pain relief after receiving conventional radiotherapy [4]. SBRT can result in longer duration of symptom relief together with improved local control and a potential for delayed disease progression [5]. The efficacy and toxicity of this treatment depend on many factors including target definition, dose fractionation, tumor volume margins, proximity to organs-at risk, and dose-delivery technique.

Currently, multiple randomized controlled trials are evaluating the effectiveness of SBRT over conventional radiotherapy in patients with bone metastases [6–8]. SBRT involves high precision dose delivery to the target volume while sparing healthy tissues. Accurate and consistent delineation of the target volume is therefore crucial in SBRT. In daily clinical practice, computed tomography (CT) is the standard imaging modality for target volume delineation in patients with bone metastases. CT offers excellent bony detail, but magnetic resonance imaging (MRI) provides increased visibility of soft tissue structures. The value of MRI in target volume definition in bone metastases is not established yet. Knowledge of the inter-observer differences in tumor volume delineation is essential to guarantee accurate and precise dose delivery. The aim of this study is to assess inter-observer agreement in delineation of bone metastases on CT, CT with co-registered MRI and MRI alone.

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Methods

This study was designed and reported according to the Guidelines for Reporting Reliability and Agreement Studies (GRRAS) [9].

Patient selection

All consecutive patients with bone metastases treated with SBRT at our center between November 2014 and December 2015 were screened for eligibility for this study. These patients are participants in the PRESENT study. The PRESENT study is a prospective cohort in which all patients with bone metastases treated at the department of radiation oncology and orthopedic surgery are enrolled [7]. Patients had to fulfill the following criteria for inclusion: bone metastases treated with SBRT, availability of CT and MR imaging in treatment position, visibility of the metastases on both imaging modalities. In case of multiple lesions, one metastasis was randomly selected for delineation.

Imaging technique and data acquisition

CT and MR imaging was performed prior to radiotherapy in treatment position. Patients were immobilized with an individual vacuum cushion (BlueBAG™, Elekta, Stockholm, Sweden). CT images were obtained with a Philips large bore CT scanner (Philips Medical Systems, Cleveland, OH) with 1 mm slice thickness. A 1.5 Tesla MRI scanner (Achieva; Philips Medical System, Best, The Netherlands) was used to acquire T1- and T2-weighted turbo spin echo (TSE) images in transverse direction for every patient. Depending on the clinically used scan protocol, coronal and/or sagittal images were acquired, including 3D T1 fast field echo (FFE) mDIXON scan with slice thickness 1.1 mm and diffusion weighted imaging (DWI) with slice thickness 4 mm (Table A1 in the online supplement). No intravenous contrast was used. The MRI to CT registration procedure consisted of defining a rectangular box of interest containing the GTV and using a mutual information registration algorithm within this volume. This method is done according to the clinical practice at our department.

Target volume delineation and observers

Five observers, two radiation oncologists and three radiation oncology residents, from three institutions independently delineated the gross tumor volume (GTV) after a training set of two patients and a subsequent consensus meeting. Three observers rated all 20 cases, and two observers from the same institution shared delineation of 20 cases (i.e. WSCE delineated case 1–13 and NK delineated case 14–20). The GTV was delineated according to our institutional protocol (Table 1), using an in-house developed delineation and data analysis software tool [10]. Observers received information about the primary tumor site, relevant medical history, location of the metastases and presenting symptoms. First, GTV was contoured on CT-images using a recommended window/level setting of 2000/500 Hounsfield units with the option to make adjustments to this setting if deemed necessary to resemble daily practice. CT delineation was followed by delineation on CT with co-registered MR images with the previous contours available. Finally, MRI delineation was performed after an interval of at least four weeks to avoid recall of prior delineations. MRI only delineations were performed on the transversel T1 image and observers were allowed to consult other sequences. Observers were instructed to record delineation time, image quality (good, moderate, poor), difficulty of contouring the target areas on all imaging modalities (five point scale: very difficult – very easy) and MRI sequences used for contouring.

Table 1
Target volume delineation in spinal and non-spinal lesions.

	Spinal lesions	Non-spinal lesions
Part of GTV	Extra-osseous disease	Extra-osseous disease Edema
Exclude from GTV	Disks Edema Osteophytes	Joints

GTV: gross tumor volume. Target volume definition according to institutional protocol and observer consensus meeting.

Data analysis

Volume of contours, conformity index and center of mass (COM) were calculated to evaluate agreement between observers and differences in location of contours. Volumes of contours were calculated per observer, per patient and per imaging modality and average volumes were computed per case and per imaging modality. To assess the overlap between all possible observer pairs, the generalized conformity index $\mathrm{CIgen} = \frac{\sum^{\mathrm{pairsij}} |Ai \cap Aj|}{\sum^{\mathrm{pairsij}} |Ai \cup Aj|}$ was calculated per case and imaging modality [11]. A CIgen of 1 implies perfect agreement among observers, while CIgen = 0 means no overlap between the delineations. For visual comparison of inter-observer agreement count maps were generated, i.e. maps of voxels showing the number of enclosing observer delineations, for each case and imaging modality.

The center of mass (COM) of each delineated volume was used to assess differences in contour locations. Differences in COM were calculated for each observer pair and were expressed as the length of a three-dimensional vector (i.e., the distance of center of the mass [dCOM]). Moreover, to provide information about the direction of variation in contour location, the maximum differences of COM between the observers in all three directions were presented.

Subgroup analyses were performed for patients with spinal and non-spinal bony lesions. The Wilcoxon signed rank test was used to analyze statistical significant differences with a p value of <0.05 indicating statistical significance.

Results

Patients and observers

Twenty consecutive patients with bone metastases treated with SBRT were included (Table 2). Most common primary tumor sites were breast ($n = 6$) and prostate ($n = 5$). The metastatic bone lesions were both spinal ($n = 11$) and non-spinal ($n = 9$).

Image quality was considered moderate to good for all CT and MR images by the observers. Observers experienced most difficulties in delineating on CT only images. Delineation on CT–MR images was considered easier than on MRI only. For each case, three to five MRI sequences were used for delineation. The transversal T1-weighted TSE (all cases, 100%), T2-weighted TSE (63/80 cases, 79%) and DWI (43/80, 54%) sequence were mostly used. Delineation time varied from 1 to 60 min per case. Contouring on CT–MR images was most time-consuming with an average of 18 min (range 3–60) per case, followed by 14 min (range 1–40) on MRI only, and 12 min (range 1–35) on CT images only.

Volumetric analysis

Tumor delineation on MR imaging resulted in significantly larger mean volumes ($45.9 \pm 52.0\ \mathrm{cm}^3$) compared to CT–MRI ($40.2 \pm 49.4\ \mathrm{cm}^3$, $p = 0.011$) and CT ($34.8 \pm 41.8\ \mathrm{cm}^3$, $p = 0.002$). (Fig. 1, Table 2). Delineations on CT–MRI were significantly larger compared to CT ($p = 0.007$).

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