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Scientific Article

The Effect of Slice Thickness on Contours of Brain Metastases for Stereotactic Radiosurgery

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Abstract

Objectives: Stereotactic radiosurgery is a common treatment for brain metastases and is typically planned on magnetic resonance imaging (MRI). However, the MR acquisition parameters used for patient selection and treatment planning for stereotactic radiosurgery can vary within and across institutions. In this work, we investigate the effect of MRI slice thickness on the detection and contoured volume of metastatic lesions in the brain.

Methods and Materials: A retrospective cohort of 28 images acquired with a slice thickness of 1 mm were resampled to simulate acquisitions at 2- and 3-mm slice thickness. A total of 102 metastases ranging from 0.0030 cc to 5.08 cc (75-percentile 0.36 cc) were contoured on the original images. All 3 sets of images were recontoured by experienced physicians.

Results: Of all the images detected and contoured on the 1 mm images, 3% of lesions were missed on the 2 mm images, and 13% were missed on the 3 mm images. One lesion that was identified on both the 2 mm and 3 mm images was determined to be a blood vessel on the 1 mm images. Additionally, the lesions were contoured 11% larger on the 2 mm and 43% larger on the 3 mm images.

Conclusions: Using images with a slice thickness >1 mm effects detection and segmentation of brain lesions, which can have an important effect on patient management and treatment outcomes.

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Introduction

Brain metastases are the most common brain tumor in adults, and the incidence is rising as patients live longer with metastatic disease.[1-3] The mounting evidence that stereotactic radiosurgery (SRS) provides good local control with limited toxicity and improved cognitive outcomes during whole brain radiation therapy has motivated the growing use of SRS for patients with brain metastases.[4] Additionally, there have been gradual shifts in patient selection criteria with ongoing trials now exploring the use of SRS in patients who present with >10 brain metastases compared with the initial trials that limited the number of brain metastases ≤4 in total.[5-7]

During patient assessment for SRS treatment, small lesions may be missed due to partial volume effects when slice thicknesses greater than the largest diameter of the tumor are used. Missed tumors may continue to grow and contribute to a poor prognosis or need for retreatment. In addition, partial volume effects can cause blood vessels to be misidentified as tumors, leading to high doses of radiation being delivered to otherwise healthy brain tissue. The American Society of Therapeutic Radiation Oncology defines SRS as "radiation therapy delivered via stereotactic guidance with approximately 1 mm targeting accuracy to intracranial targets in 1 to 5 fractions."[8] Target lesions are commonly identified and assessed on magnetic resonance images (MRI) due to the superior soft tissue contrast compared with computed tomography (CT). Owing to the highly conformal nature of SRS dose delivery, the volume of the contoured target defines the dose delivered to the metastasis. Tumor contours that do not encompass the whole lesion volume will yield suboptimal dose to the metastasis, whereas tumor contours that are larger than the true lesion volume will result in unnecessarily high doses to the surrounding normal tissue. Therefore, the effect of the accuracy of target definition on achieving tumor control while sparing the surrounding healthy brain tissue is magnified for SRS.

The typical imaging workflow for the management of brain metastases treated with SRS includes acquisition of a diagnostic MRI to determine patient eligibility, a planning CT and possibly dedicated planning MRI on the day of treatment, and MRIs periodically after treatment to evaluate tumor response. Diagnostic MRIs are commonly acquired with a slice thickness of >2 mm, which may miss small lesions.[9] In contrast, a planning MRI typically is acquired with 1-mm isotropic voxels and therefore may reveal additional small lesions that were undetected on the diagnostic images.[10,11] Based on the number and distribution of these additional metastases, the patient may require a longer treatment than originally scheduled, or possible an alternative treatment plan altogether.[12,13] However, a dedicated planning MRI is often not acquired, leading physicians to plan on images acquired for diagnostic purposes.[14] Planning on images with a slice thickness of ≥2 mm may affect both lesion detection and accuracy of contouring. Similarly, follow up diagnostic MRIs acquired with a slice thickness >2 mm may reduce the accuracy of assessment of tumor burden and quantification of therapeutic outcomes.[15]

The major cost of acquiring high-resolution MR images is time. A change from 2 mm to 1 mm slice thickness can double the scan time required to generate an equivalent signal to noise ratio in each voxel, assuming no other parameters are changed. Therefore, evidence of a substantial effect on patient treatment is desired to justify the use of 1 mm thickness into the clinical workflow. This study quantitatively evaluated the effect of slice thickness on 2 aspects of SRS treatment: lesion detection and lesion segmentation (ie, contours).

Methods

Phantom study

We scanned the large ACR MRI Quality Assurance Phantom (J.M. Specialty Parts, San Diego, CA) and the ISMRM/NIST System Phantom (System Phantom Model 130, High Precision Devices, Inc, Boulder, CO) phantoms on the same MRI scanner and with the same protocol used for the patient scans in this study. In addition, we acquired the same protocol with a slice thickness of 2 mm and 3 mm. The 1 mm slice-thickness images were then resampled to 2 mm and 3 mm slice thickness in the same manner as the clinical images and compared with the images acquired with a 2- and 3-mm slice thickness. The images were analyzed in RayStation.

A quantitative measurement of the slice thickness was performed using the ramps in the ACR phantom. We determined the slice thickness in each image set by measuring the length of the ramp in the image with a window setting of 1 and a level of half the maximum pixel value in the ramp and dividing by 10.

The ISMRM phantom was used to measure the contoured volume as a function of slice thickness. Four 1 cm diameter and 3 1.7 cm diameter contrast-filled spheres were contoured in the axial plane on each image set. The average region of interest (ROI) volume for each sized sphere was compared across the image sets.

Patient eligibility

Under institutional review board approval (PA18-0832), 30 consecutive patients treated with their first or only Gamma Knife stereotactic radiosurgery treatment in a Leksell Coordinate G Frame (Elekta, Stockholm, Sweden) using 3 Tesla (T) MR imaging for target delineation of ≥1 brain metastases between April 2018 and February 2019 were included in this study. Two patients were excluded from this cohort because they were simulated on a 1.5 T machine, leaving 28 patients for analysis in the final data set.

Treatment planning images

All patients were treated on an Elekta Gamma Knife Perfexion (Elekta, Stockholm, Sweden). On the day of treatment, patients were imaged on a GE Discovery 750 or 750W 3T MRI system (GE Healthcare, Chicago, IL) for treatment planning. Imaging was performed with a Leksell Coordinate G Frame attached to the patient's skull. Treatment planning imaging consisted of an axial 3-dimensional fast spoiled gradient echo (FA = 12, TR = 6.65 ms, TE = 1.99 ms, N = 1) with a 0.9375 mm in-plane resolution and contiguous 1 mm slice thickness acquired after intravenous injection of MultiHance (gadobenate dimeglumine) at a dose of 0.1 mmol/kg.

Image analysis

The treatment planning images were downloaded from GammaPlan (Elekta, Stockholm, Sweden) for processing in Python. To simulate the acquisition of images with contiguous slice thicknesses of 2 mm, every 2 slices of the 1 mm images were averaged along the slice direction. To simulate the acquisition of contiguous 3 mm slices, every 3 slices were averaged along the slice direction. The 3 image sets were then reimported to GammaPlan as a new patient without the original contours.

All 3 image sets were contoured by 2 radiation oncologists with experience in Gamma Knife treatment planning. To reduce the chances of recalling a previously contoured patient, the 3 mm images were contoured first, then the 2 mm images, then the 1 mm images, throughout several weeks. The images and contours were then moved to RayStation (Raysearch, Stockholm, Sweden) for analysis. The contours on the 1 mm images were used as the gold standard against which the contours on the 2 mm and 3 mm images were compared. Metastases were identified across images according to their location.

We evaluated the number of metastases found on the 1 mm images but missed on the thicker slice images and the number of cases in which normal tissues were misclassified as metastases on the thicker slices. We also evaluated the contoured volume of each metastasis on each of the 3 image sets.

Results

Phantom image analysis

A qualitative comparison of the images is presented in Figure 1. The resampled images had less partial volume artifacts in the axial plane and Gibbs artifacts in the coronal plane than the corresponding acquired images. These artifacts are averaged out in the resampled images. The effect of thicker slices on the contours can be observed in both the acquired and resampled image sets but is qualitatively worse in the acquired data sets.

The measurements of the slice thickness from the ACR ramps are presented in Table 1. The measured slice thickness was slightly higher than the nominal slice thickness in all the images. The difference was greater for the image sets acquired with a thicker slice than those that were resampled to a thicker slice.

The average volume of the contours of the contrast-filled spheres in the ISMRM/NIST phantom are presented in Tables 2 and 3. For the small spheres, the average

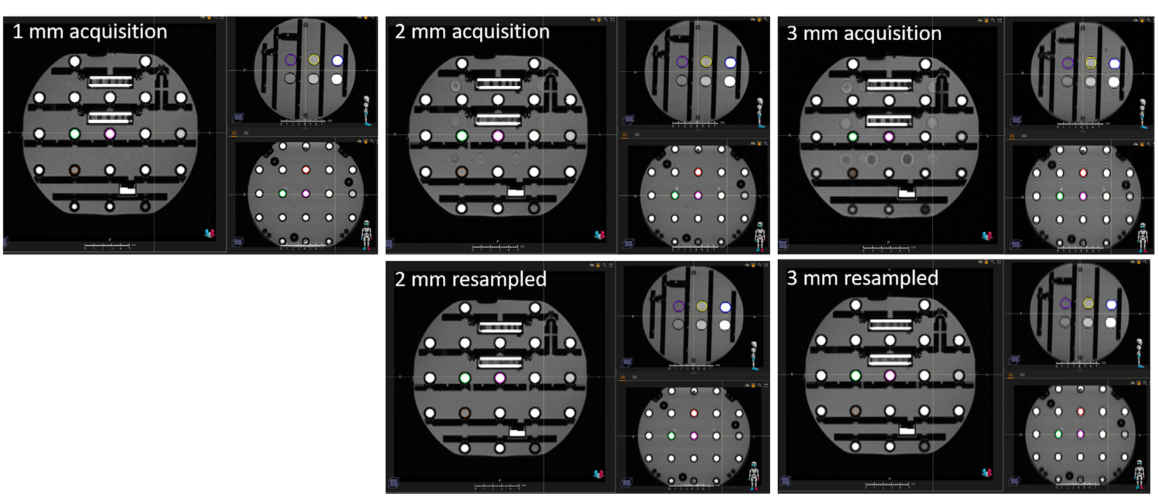

Fig. 1 (Top row) Axial, sagittal, and coronal views of the ISMRM/NIST phantom scanned on the clinical magnetic resonance imaging with the clinical protocol with 1 mm, 2 mm, and 3 mm slice thickness. (Bottom row) Simulated thick-slice acquisition images composed by averaging every 2 and every 3 slices of the 1 mm acquisition scan. Contours used for volumetric analysis are shown.

Table 1 The full-width-half-maximum of the slice thickness profile acquired from the ramps in the ACR phantom

Nominal slice thickness	1 mm	2 mm	3 mm
Measured on acquired image	1.25 mm	2.31 mm	3.32 mm
Measured on resampled image	N/A	2.18 mm	3.03 mm

Table 2 The average volume of the contours of four 1 cm-diameter spheres on acquired and resampled images

Small sphere average volume (cm^3)			
Nominal slice thickness	1 mm	2 mm	3 mm
Measured on acquired image	0.58	0.59	0.61
Measured on resampled image	N/A	0.57	0.59

Table 3 The average volume of the contours of three 1.7 cm-diameter spheres on acquired and resampled images

Large sphere average volume (cm^3)			
Nominal slice thickness	1 mm	2 mm	3 mm
Measured on acquired image	2.63	2.64	2.65
Measured on resampled image	N/A	2.60	2.52

contoured volume was slightly larger on the images acquired with a 2 mm or 3 mm slice thickness than on the 1 mm images. For the resampled images, the 2 mm-slice thickness had a slightly smaller average contoured volume, and the 3 mm-slice thickness images had a slightly larger contoured volume. The differences were greater for the images acquired at 2- and 3-mm slice thickness than for the corresponding resampled images.

Patient cohort

The study included 28 patients: 13 (46%) men and 15 (54%) women. The distribution of primary malignancies is presented in Table 4. The study group consisted of a total of 102 metastases, 89 (87%) of which were 1 cm^3 or smaller, as shown in Figure 2.

Table 4 Distribution of site of primary malignancy for the 28 patients in the study

Primary malignancy site	No. of cases (percentage of sample)
Melanoma	10 (36)
Lung	9 (32)
Breast	5 (18)
Kidney	2 (7)
Esophageal	1 (3.5)
Uterine	1 (3.5)

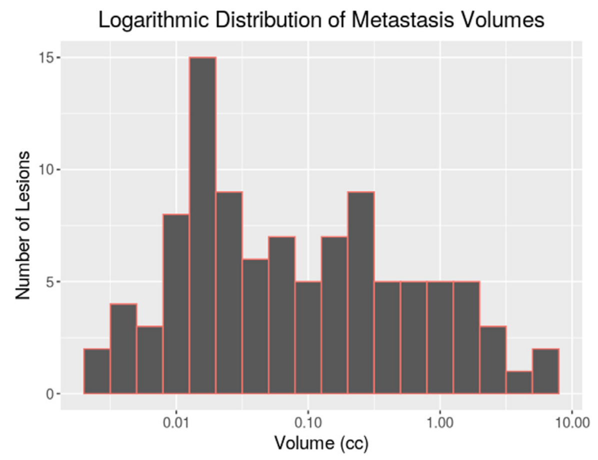

Fig. 2 A histogram of the volume of each lesion found on the images with 1 mm slice thickness.

Effects on lesion detection

One hundred and two lesions were contoured on the images with 1 mm slice thickness. 13 metastases in 7 different patients were missed on the 3 mm images. Three metastases in 3 different patients were missed on the 2 mm images. All metastases missed on the 2 mm images were also missed on the 3 mm images. The average volume of the lesions missed on the 2 mm images was 0.006 cm^3 (range, 0.004-0.008 cm^3). The average volume of the lesions missed on the 3 mm images was 0.016 cm^3 (range, 0.003-0.060 cm^3). An example case in which the lesion was not identified on the 2 mm and 3 mm images is shown in Figure 3. One lesion was contoured on the 2 mm and 3 mm images but was determined to be a vessel on the 1 mm images, as shown in Figure 4.

Effects on contoured volume

The difference in the contoured volume of lesions on the 2 mm and 3 mm slice thickness images from the 1 mm slice thickness images is shown in Figure 5. Of the 99 lesions contoured on the images with a 2 mm slice thickness, the mean percent difference from the volume contoured on the 1 mm slices was 10.7%, with a maximum of 186.5% and a minimum of −60.32%. In addition, 63 lesions (64%) were contoured larger on the 2 mm images than they were contoured on the 1 mm images. Of these, the mean difference was 0.055 cm^3, with a maximum difference of 0.5 cm^3. The remaining 36 (36%) lesions were contoured smaller on the 2 mm images than on they were contoured on the 1 mm images, with a mean difference of −0.026 cm^3 and a maximum difference of −0.51 cm^3.

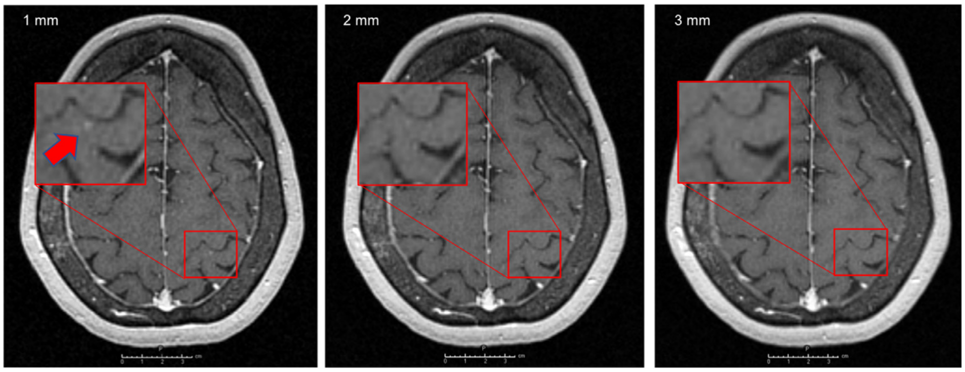

Fig. 3 The original planning image (left), showing a metastasis (red square) that was not detected on the images when resampled to simulate an acquired slice thickness of 2 mm (middle) and 3 mm (right).

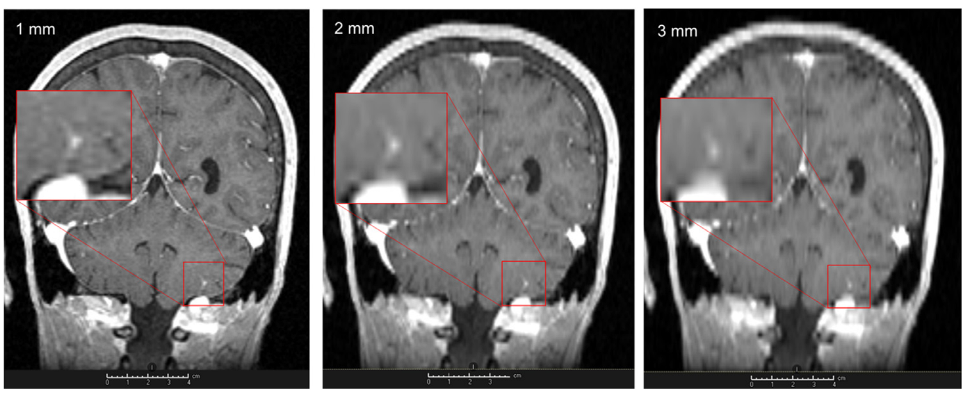

Fig. 4 The original planning image (left) showing a blood vessel (red square) that was identified as a metastasis on the 2 mm (center) and 3 mm (right) resampled slice thicknesses.

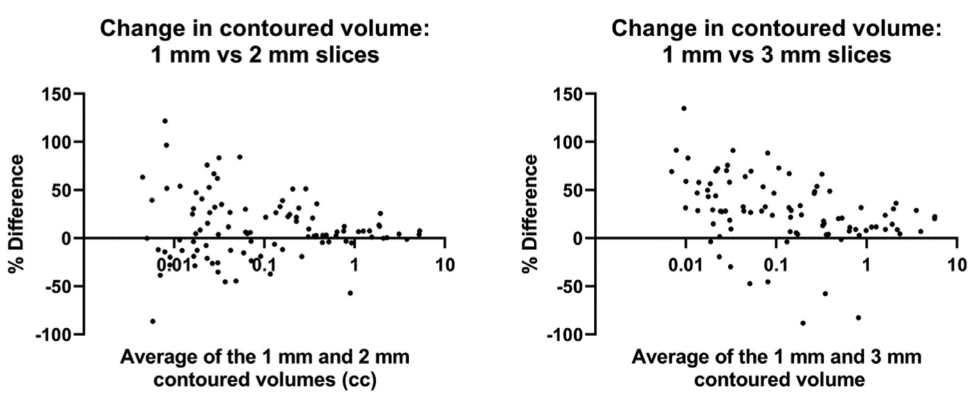

Fig. 5 A Bland-Altman plot of the relative difference in volume between lesions contoured on the 2 mm images and 3 mm images from those on the 1 mm images. A positive percent difference indicates that the lesion was contoured larger on the resampled image.

Of the 89 lesions contoured on the 3 mm images, the mean percent difference in volume compared with the lesions contoured on the 1 mm images was 43.5% and ranged from −61.2% to 415.0%. In addition, 79 of the lesions contoured on the 3 mm images (88%) were contoured larger than they were contoured on the 1 mm images, with a mean difference of 0.12 cm^3 and a maximum difference of 1.27 cm^3. The remaining 10 lesions (11%) were contoured smaller on the 3 mm images than on the 1 mm images, with a mean difference of −0.11 cm^3 and a maximum difference of −0.67 cm^3.

Discussion

The ability to detect and segment brain metastases accurately is critical to delivering effective radiosurgery treatment for brain metastases. Prior work has been done to determine optimal imaging acquisition parameters for SRS planning, with the consideration of tradeoffs of cost and scan time required to achieve high-quality images. Concerning magnet strength, 3T has been shown to have superior tumor contrast to 1.5T.[16,17] Magnetic field strengths >3T have not demonstrated additional improvement in tumor visualization, but small blood vessels become visible.[18] Others have demonstrated improved detection and visualization of small lesions when contrast agents with high relaxivity, such as gadobutrol, are used in higher concentrations.[19] Some institutions use high-dose contrast agents for SRS planning with the goal of detecting and targeting all metastases at the time of treatment.[17,20,21]

In general, contiguous thin slices are recommended for imaging brain metastases, but the definition of a thin slice has been interpreted to be anywhere between 1 mm and 2.4 mm.[9,22,23] Prior work has shown a slight improvement in the detection of metastases on 2 mm continuous slices relative to images with 5 mm and 7.5 mm spacing.[11] Although the planning software for Gamma Knife requires square pixels and recommends contiguous slices, other modalities such as conventional linear accelerator (LINAC)-based treatments may allow variations in the voxel dimensions. The findings presented here that contoured volume increases with slice thickness agree with previously reported in phantom studies.[24]

The purpose of the phantom study was to demonstrate that thick-slice acquisitions could be appropriately approximated by averaging subsequent slices in a thin-slice image. Overall, our results showed that averaging subsequent slices produces higher quality images than would be acquired at this slice thickness. This is because the averaged images essentially contain more data because each slice averages multiple measurements. This is analogous to increasing the number of averages for the thicker slice acquisitions. However, we chose not to do so in this study because clinically thicker slices are used to decrease scan time, so increasing the number of averages per slice would negate the benefit compared with 1 mm slices.

As it relates to the work in this study, this data show that our method at worst underestimates the negative effects of thick slice acquisitions for SRS treatment planning. Because prospectively acquiring 3 separate scans before SRS would be infeasible, this approach is an adequate substitution.

The findings of this study demonstrate that even within the prior reported range described as thin slice MR, using slice thickness greater than 1 mm during imaging can reduce the detection and accuracy of the segmentation of brain metastases. In our cohort of 28 patients, at a slice thickness of 2 mm, 4 patients (14%) either had lesions missed or normal tissue misidentified as a lesion; 7 patients (25%) had missing or misidentified lesions when the images had a slice thickness of 3 mm. These effects have important implications in SRS treatment planning because small lesions that are missed can develop into symptomatic disease later, potentially needing radiation therapy or additional interventions, which could involve another frame placement and result in added cost to the system and inconvenience to the patient. Misidentifying blood vessels as lesions will lead to this normal tissue receiving high doses of radiation unnecessarily, which could cause adverse side effects.

The results of this study also have important ramifications outside of SRS treatment planning. Often, diagnostic MR images used for treatment or for posttreatment follow up are acquired with slice thicknesses greater than 1 mm. Our results indicate that if an image with a large slice thickness is used for pretreatment evaluation, small lesions can be missed, and patients may be excluded from receiving SRS who would otherwise be candidates. Similarly, there is a chance that MRI with slice thickness greater than 1 mm may not identify patients with numerous tiny metastases and may lead to an aborted SRS treatment when thin slices are acquired on the day of treatment after frame placement.[25] When thick-slice images are used in follow-up, small lesions may be missed entirely or the lesion volume may be overestimated, making it appear to have grown. These effects should be considered when making pre- and posttreatment decisions based on thick-slice diagnostic images, and when possible 1 mm slice thickness or less should be used. This conclusion is supported by consensus recommendations such as the Brain Tumor Imaging Protocol-Brain Metastases (BTIP-BM), which recommends a 3-dimensional T1 postcontrast MRI with a 1 mm slice thickness for diagnostic and follow-up imaging.[10]

On average, increasing the slice thickness led to an increase in the contoured volume of the lesion. This effect was more pronounced at larger slice thicknesses and for smaller lesions. The large variation in the contoured volume of small metastases is inherent to their small volume because small absolute changes in volume will cause large percentage change. Most of the differences in volume were due to the extent of the contour in the slice direction, but some differences were in the axial direction due to partial volume effects. When the size of the lesion approaches the size of the slice, the effect of slice thickness will depend on where the lesion falls in the slice sampling. In SRS planning, due to the high dose gradient on the edge of the target, the contoured volume of the lesion is tightly tied to the dose delivered to the lesion. Therefore, overestimating the volume of a lesion can lead to delivery of unnecessarily high radiation doses to the surrounding normal brain tissue. Conversely, underestimating the volume of a lesion can lead to undertreatment, which increases the chances of local recurrence. Total tumor volume may be a more significant measure of burden than the number of metastases,[26] making an accurate measurement of volume even more critical for determining patient candidacy and evaluating posttreatment response.

Of course, slice thickness is not the only scan parameter that can affect the detection of metastases. Previous work has shown that scans at 3T can improve the detection of small tumors and visualization of blood vessels.[16,17] Although scans at 3T are more susceptible to artifacts or geometric distortion, these are mitigated by the small field of view and postprocessing, and this may be outweighed by the improvement in sensitivity.[27] The pulse sequence type is also important. Gradient echo sequences have been shown to be superior for small tumor detection than spin echo sequences, largely due to the superior resolution for a given acquisition time, especially in the slice direction.[12] Interobserver variability has also been shown to have an even greater effect on the contoured volume of brain metastases than seen in this work.[28] Each of these effects is important to consider and aim to mitigate when developing a protocol for SRS treatment planning.

This study has several limitations given its retrospective nature. First, the 2 mm and 3 mm slice images were synthetically generated from the 1 mm images, rather than acquired independently. Acquiring consecutive images with varying slices thickness would have created bias due to the build-up and clearance of contrast from one scan to the next. The synthetic generation of images ensured the same level of contrast in all images for the same patient while providing an appropriate approximation of similarly acquired images as demonstrated by the phantom studies. However, this method did limit the range of resolutions that could be analyzed to greater than the 1 mm data set. In clinical practice, diagnostic images with thick slices also have an in-plane resolution less than 1 mm. Future work should be done to confirm that our conclusions hold for images with <1 mm in-plane resolution. Additionally, the contours were drawn on all 3 slice thicknesses and reviewed by only 2 radiation oncologists, which may lead to some unintended bias toward these oncologists' preferences. Although measures were taken to minimize the chance that the physician remembered cases across slice thicknesses, it is impossible to rule out the possibility completely. However, this effect would reduce the difference between the 3 slice groups, not increase them. In clinical practice physicians may contour slightly larger if they know they are working on thick-slice images. In this study the physicians were aware of the slice thickness of the images they were contouring but did not contour larger on the thicker slice images, as they were aware of the study's aim. Future work should be done with multiple observers to confirm that these results are consistent across users. Finally, although it is known that dose is dependent on contoured volume, future work needs to be done to determine the magnitude of the dosimetric effect of the volume differences we have shown here.

Conclusions

We have shown that using MR images with a slice thickness >1 mm for the consideration and treatment of patients with SRS for brain metastases can lead to missed and overcalled lesions and affect the volume of segmented lesions, which can have an important effect on patient management and treatment outcomes. These findings should be considered when images are used to select patients for treatment, planning, and evaluating posttreatment response.[10]

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