Re: Magnetic Resonance Imaging Underestimation of Prostate Cancer Geometry: Use of Patient Specific Molds to Correlate Images with Whole Mount Pathology

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To the Editor: Priester et al add to the message of others underlining that magnetic resonance imaging (MRI) underestimates the size and extent of prostate tumors. Indeed, all macroscopic estimation of any tumor will underestimate histological tumor extent, which, after all, is why we apply a margin to the excision of any solid tumor. The data presented are concordant with data previously reported in The Journal that emphasize the importance of accurate registration between the in vivo and ex vivo excised prostate.[1]

Everybody agrees that this undertaking is challenging. We suggest that the methods reported by the authors may not be optimal in addressing this challenge. Our first observation relates to the cut of the specimen at a 4.5 mm interval. Noguchi et al reported a significant overestimation in cancer volume at radical prostatectomy analysis when the slice thickness was increased from 3 mm to 6 mm.[2] In the current study MRI was acquired with 1.5 mm slice thickness, a threefold difference compared to the step section pathology. This discrepancy serves to systematically bias the estimate of "histological volume" in an upward direction and widens the apparent discrepancy with any MRI derived volume. Moreover, the performances of the 2-dimensional axial "elastic" registration are not disclosed or assessed with usual metrics for residual error or overlap.[3,4] The reader is unable to attribute discrepancies to either cancer geometry or registration method.

In addition, use of a mold as a stand-alone tool has yet to be assessed for the purpose of 3-dimensional volumetric and spatial coregistration. The authors rightfully acknowledge the work of Turkbey et al in this space.[5] However, Turkbey et al used the mold to facilitate detection, a binary challenge, not volume and geometry estimation. The observation in the current study, that excised prostates are on average 7% larger than predicted on MRI, runs contrary to the experience of others, who tend to observe a 20% decrease in volume against MRI estimates.[6] A prostate that is larger than the mold created for it will not fit easily, and if forced to fit, will undoubtedly distort. Some authors have recently reported the usefulness of other sequences of multiparametric MRI,[7,8] such as dynamic contrast enhanced imaging, to establish the necessary target volume for focal therapy, while Priester et al based their assessment on T2-weighted imaging only in a bias population undergoing radical prostatectomy.

This field clearly remains a challenging area of research endeavor. No group seems to have gotten it right, which might explain the contradictory data that we have at our disposal.[9] For instance a recent study, using different methodology, demonstrated that MRI underestimated tumor volume by only 4%,[10] compared to the 300% or so claimed by Priester et al.

Respectfully,

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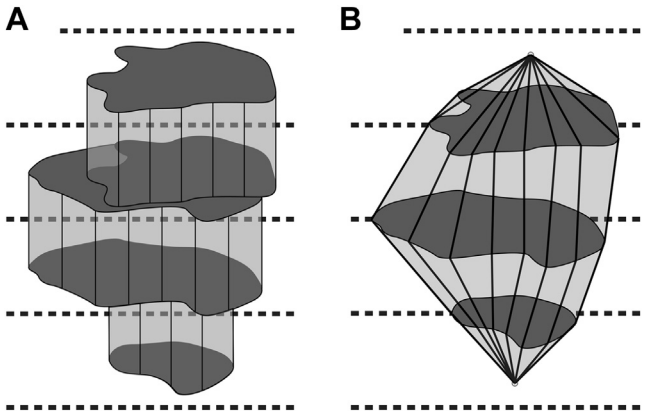
Reply by Authors: The low through-plane resolution of whole mount slides can cause overestimation of tumor volume, especially when calculated as "the sum of tumor areas at different levels multiplied by the section thickness."[2] This method extrudes outward even at the far apex and base (part *A* of figure). By comparison, we interpolated between contours and tapered the extrusion at the far apex and base (part *B* of figure), refining and decreasing the volume estimates.

The performance of our registration methodology was not disclosed or assessed, a limitation that was acknowledged in our discussion. Ten prostates have subsequently been scanned ex vivo within the mold, enabling assessment of the registration accuracy of the mold (unpublished data). Landmarks delineated in that study indicated a mean in-plane registration error of 3.3 mm, which could only account for a small portion of the discrepancy between MRI contours and whole mount tumors.

Orczyk and Emberton also observed that the 7% underestimation of prostate volume on MRI could cause distortion of glands within the mold. However, specimens were weighed before shaving of the apex and base, and volume was therefore reduced before placement in the mold. The majority of specimens fit easily within the mold without noticeable distortion.

We agree that data in this field are highly variable and often contradictory. Comparison between studies is difficult since MRI and registration methodologies vary widely. Few groups have reported volume underestimation as dramatic as ours, a discrepancy that can partly be attributed to the MRI contouring technique. As discussed in our article, the fidelity of prostate MRI can be improved through incorporation of additional MRI sequences, revision of contouring techniques and use of tracked biopsy information.



Tumor reconstruction using simple extrusion method (*A*) vs interpolated and tapered method (*B*). Dark gray shading indicates tumor contours. Light gray shading signifies reconstructed volumes. Dashed lines indicate whole mount slice positions.

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