Tumor Target Volume for Focal Therapy of Prostate Cancer—Does Multiparametric Magnetic Resonance Imaging Allow for a Reliable Estimation?

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Abbreviations and Acronyms

ADC = apparent diffusion coefficient
DCE = dynamic contrast enhanced
DW = diffusion weighted
K_{trans} = transfer constant
mp = multiparametric
MPV = mp tumor volume
MRI = magnetic resonance imaging
PZ = peripheral zone
T2W = T2-weighted
TV = target volume
TZ = transition zone

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Purpose: We determined whether endorectal multiparametric magnetic resonance imaging at 1.5 Tesla could predict tumor target volume in the perspective of focal therapy of prostate cancer.

Materials and Methods: A total of 84 consecutive patients underwent multiparametric magnetic resonance imaging before radical prostatectomy. The volume of each suspicious area detected on magnetic resonance imaging and of all surgical histological foci was determined by planimetry. We first used each magnetic resonance imaging sequence (T2-weighted, diffusion weighted and dynamic contrast enhanced) and then the sequence showing the largest tumor area (multiparametric volume). Finally, the largest area of any sequence was used to calculate a target volume according to the volume of a cylinder. Agreement between magnetic resonance imaging and pathological findings was assessed by linear regression and residual analysis.

Results: Histology revealed 99 significant tumors with a volume of greater than 0.2 cc and/or a Gleason score of greater than 6. Of the tumors 16 (16.2%) were undetected by multiparametric magnetic resonance imaging. Linear regression analysis showed that tumor volume estimated by T2-weighted or diffusion weighted imaging correlated significantly with pathological volume (r^2 = 0.82 and 0.83, respectively). Residuals from diffusion weighted imaging volume estimations did not significantly differ from 0. Nevertheless, diffusion weighted imaging underestimated pathological volume in 43 of 87 cases (49%) by a mean of 0.56 cc (range 0.005 to 2.84). Multiparametric and target volumes significantly overestimated pathological volume by a mean of 16% and 44% with underestimation in 28 (32%) and 15 cases (17%), respectively. Volume underestimation was significantly higher for tumor foci less than 0.5 cc. The percent of Gleason grade 4 did not influence tumor volume estimation.

Conclusions: Magnetic resonance imaging can detect most significant tumors. However, delineating a target volume may require further adjustment before planning magnetic resonance imaging targeted focal treatment.

Key Words: prostate, prostatic neoplasms, magnetic resonance imaging, diagnostic imaging, prostatectomy

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PROSTATE mp-MRI combining T2W, DCE and DW-MRI is highly accurate to detect and localize tumor foci greater than 0.2 cc[1] and high Gleason grade foci.[2] Thus, mp-MRI could be potentially used in the pretreatment evaluation and guidance of focal therapy.[3,4] However, mp-MRI has limited accuracy[5–8] to precisely measure tumor volume. As a result, currently evaluated focal treatments consist of prostate hemiablation. To our knowledge no attempt has been made to estimate a TV representing the area to be treated plus a safety margin, as in radiation therapy.

Therefore, using radical prostatectomy as the reference standard we evaluated the accuracy of mp-MRI to estimate tumor volume. We then assessed whether a TV rather than the tumor volume could be defined in the perspective of focal treatment aiming to ablate the tumor without leaving tumor foci outside the treated area.

PATIENTS AND METHODS

A total of 95 consecutive patients presenting with a clinical stage lower than T3 prostate cancer underwent mp-MRI before radical prostatectomy between January 2009 and March 2010. Of the patients 11 were excluded from the study due to a greater than 8-month delay between MRI and surgery (2), previous biopsy (3), motion artifact (3) or a radical prostatectomy specimen not suitable for adequate correlation (3). The remaining 84 patients were included in analysis. The institutional review board issued a waiver of informed consent to review MRI, clinical and pathological data.

MRI was performed at least 6 weeks after biopsy to minimize biopsy artifact. MRI was done with a 1.5 Tesla Avanto magnet (Siemens Healthcare, Erlangen, Germany) and an integrated endorectal-pelvic MR Innerva phased array coil (Medrad, Pittsburgh, Pennsylvania) (table 1). The endorectal coil was inserted and inflated with 80 to 100 ml of air. DW images had the same orientation as transverse T2W images. DCE data were post-processed with a pharmacokinetic model (iCAD, Nashua, New Hampshire) based on the model of Tofts et al[9] to estimate tissue physiological parameters, including K_{trans} and k_{ep} (rate constant). We also calculated the initial gadolinium concentration AUC for the first 60 seconds after contrast arrival. Surface area was measured on color coded parameter maps.

MRI was interpreted by a consensus of 2 experienced radiologists (FC and GK) blinded to pathological findings. Cancer was suspected in cases of nodular or mass-like low signal intensity on T2W or DW-MRI with or without early enhancement on DCE (figs. 1 to 3). T2W, DW and DCE-MRI volumes were calculated separately by planimetry (tumor area on each slice level × slice thickness [3.5 mm] × number of slices showing tumor) (fig. 4). On DCE images the color coded parameter showing the largest area was chosen. Planimetry was then repeated with the MRI sequence (T2W, DW or DCE) showing the largest tumor area on each slice level. Tumor volume calculated with this single area per slice was termed MPV (fig. 4). The last calculated volume only considered the largest tumor area visible on any MRI sequence and the number of slices showing tumor to calculate a volume denominated TV (fig. 4). Five volumes (T2W, DW, DCE, MPV and TV) were measured and compared to pathological volume.

India ink coated specimens were fixed in formalin for at least 48 hours. The glands were cut into 4 mm sections perpendicular to the posterior plane, including the apex and base according to a modified Stanford protocol, and labeled. As derived from neuropathology protocols, the tissue processing protocol is slow (20 hours), which substantially limits tissue shrinkage. Paraffin embedded blocks were cut to produce 5 μm whole mount sections, which were allowed to expand in 37C warm water and then stained with hematoxylin and eosin. All slides were digitized with a high resolution scanner (Hamamatsu, Hamamatsu City, Japan).

A single experienced uropathologist (FB) blinded to MRI findings reviewed all samples and manually outlined each tumor focus using the software electronic mapping tool (Hamamatsu). The total number and sites of tumor foci were recorded. If the distance between 2 tumor foci was greater than 4.5 mm, they were considered separate foci.[10] Tumor foci were graded according to the modified Gleason grading system and the percent of grade 4 was recorded.[11] Pathological stage was determined according to the 2002 TNM classification.[12]

Tumor volume was calculated by computerized planimetry. Preliminary analysis of the first 15 specimens showed no difference in prostatectomy specimen volume before vs after fixation. Therefore, we did not consider it necessary to include a tumor shrinkage factor, as did others.[5] Tumor foci were considered clinically insignificant if they were organ confined with a volume of less than 0.2 cc and a Gleason score of 6 or less. We chose the threshold of 0.2 cc since it can be accurately detected by

Table 1. *MRI protocols*

Sequence*	T2W-MRI 3-Dimensional Acquisition	DW-MRI Echoplanar Imaging†	DCE-MRI T1-Weighted Gradient Echo
Slices (mm thick/No.)	1 (224)‡	3.5 (20)	3.5 (20)
Repetition time/echo time (msecs)	1,200/120	3,700/104	5.1/1.85
Voxel resolution (mm^3)	0.8 × 0.8 × 1	1.3 × 1.3 × 3.5	1.25 × 1.25 × 3.5
Temporal resolution (secs)	Not applicable	Not applicable	8.5§
Acquisition time (mins)	5	5	5

* Field of view 20 cm.
† Acquisition with several b values (100, 200, 400 and 800).
‡ Covered volume from pubic bone to aorta bifurcation.
§ Intravenous gadolinium bolus injection (0.2 ml/kg at 3 cc per second).