Multiparametric Magnetic Resonance Imaging of the Prostate

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Implementing multiparametric magnetic resonance (MR) imaging has broadened MR use and has gained importance in the early detection of neoplasia. Together with rectal examinations and prostate-specific antigen tests, multiparametric MR imaging helps to identify suspicious lesions that require histological examination and to follow up on low-grade tumors. It also can reduce overdetection of indolent cancers observed during prostate-specific antigen tests. Multiparametric MR imaging improves the diagnostic and therapeutic paradigm of prostate cancer by increasing the accuracy of diagnostic data.[1]

McNeal's division of the prostate into zones is visible in T2-weighted MR imaging (see **Figure 1**).[2] In the cranial to caudal direction, the prostate gland is identified as the base (directly under the bladder), the midzone, and the apex. From a histological perspective, the gland is divided into these 4 main zones:

- anterior fibromuscular band (partially connected to the detrusor muscle of the bladder wall)
- central zone (surrounding the ejaculatory ducts)
- peripheral zone
- transition zone (surrounding the urethra)

Historically, the central and transition zones were identified commonly on MR images as a central gland, given the low to intermediate signal in T2-weighted images. Today, however, MR imaging can differentiate the central zone and the transition zone, as the central zone appears as an area of homogeneous low signal in most patients. Therefore, the term *central gland* should be avoided.[3]

In axial T2-weighted images, the peripheral zone appears as a homogeneous hyperintense half-moon–shaped tissue, positioned in the posterior-lateral zone of the gland. The neurovascular bundles are located on the lateral posterior zone and represent a major route of extraprostatic extension.[4]

MR Protocols for Prostate Imaging

MR imaging protocols for the prostate are based on the fundamental principle of multiparametric imaging, which combines high-resolution anatomical images (T2-weighted images) with functional imaging obtained with diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MR. Additional (eg, T1-weighted sequences) and functional MR spectroscopy imaging anatomical sequences can be performed based on the clinical indication. Avoiding unnecessary sequences is important because they can lengthen the duration of the study, intensify an overwhelming sensation (eg, patients with a claustrophobia), and can reduce compliance with positioning directions. Each protocol might be tailored to the specific patient, the clinical indication, and the equipment available.

Although 1.5 T scanners initially are used, using 3 T scanners is becoming more common for the multiparametric MR imaging studies of the prostate, both for research purposes and clinical applications.[5,6] The main advantage of using a 3 T scanner is the signal : noise ratio (SNR) increase. SNR increases when the magnetic field strength increases. When switching from a 1.5 T to a 3 T scanner, the SNR doubles. This increase can

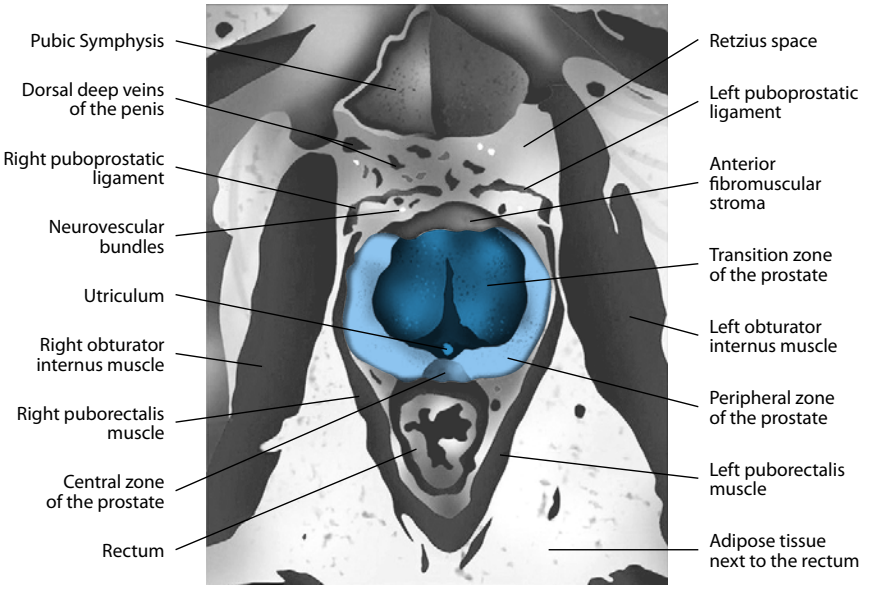

Figure 1. *Axial magnetic resonance (MR) image of the prostate and surrounding area with anatomy labeled. Figure courtesy of the author.*

improve some technical aspects such as imaging quality; the increased SNR reduces the acquisition voxel size by improving the special resolution of the anatomical T2-weighted images. This leads to an increase of the definition of the prostate on an anatomical and pathological level. Finally, a high SNR reduces the scan time, and therefore improves the dynamic contrast-enhanced MR imaging temporal resolution.

However, using a 3 T magnetic field also presents some technical challenges. The radiofrequency energy-inducted deposition (quantified by the specific absorption rate) increases with the squared force of the main magnetic field, and the deposited energy multiplies by 4 with a 3 T magnetic field.[7] Modifying the conventional parameters of some sequences to meet the limitations of the exposure is necessary. For example, the T2-weighted fast spin-echo sequences can be modified by partially refocusing instead of a full variable flip angle for the specific absorption rate to be reduced. A lower magnetic field strength (1.5 T) is preferable when a patient has metal implants, such as leg prosthetics, to minimize magnetic susceptibility.[8] Scanners lower than 1.5 T should be avoided given the low anatomical resolution of sequences obtained with weaker magnetic fields.

Patient Preparation

There are 3 approaches to the study of the prostate:

- dedicated endocavitary receiver coil (ie, endorectal coil) (see **Figure 2**)
- multichannel phased-array coil (ie, torso coil) (see **Figure 3**)
- combination of the 2 in multicoil mode (see **Figure 4**)

An endorectal coil can increase the potential effects of intestinal motility, which undermines the quality of the images.[9] This approach also can cause discomfort during insertion and jeopardize the time patients can tolerate being inside the magnet bore. The multichannel phased-array coil (ie, torso coil) is preferable because it produces high-quality images and an excellent SNR.

Patients should be briefed on how to prepare for the examination. Preparation can include enemas the night before and the morning of the examination and fasting for 6 hours before imaging.[10] Patients will be given a disposable gown and shoe covers to wear with their undergarments. They also will be asked to urinate to prevent variation in the relationship among the internal organs during imaging. Then the health care staff will obtain a peripheral venous access with a 18-20 gauge

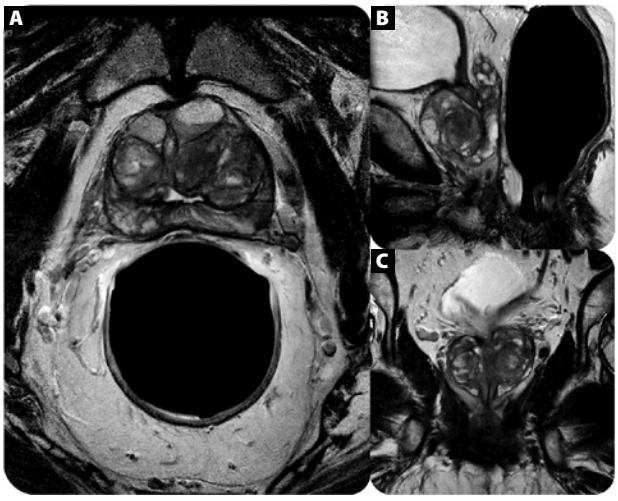

Figure 2. *T2-weighted axial (A), sagittal (B), and coronal (C) MR images of the prostate using the endorectal coil. Images courtesy of the author.*

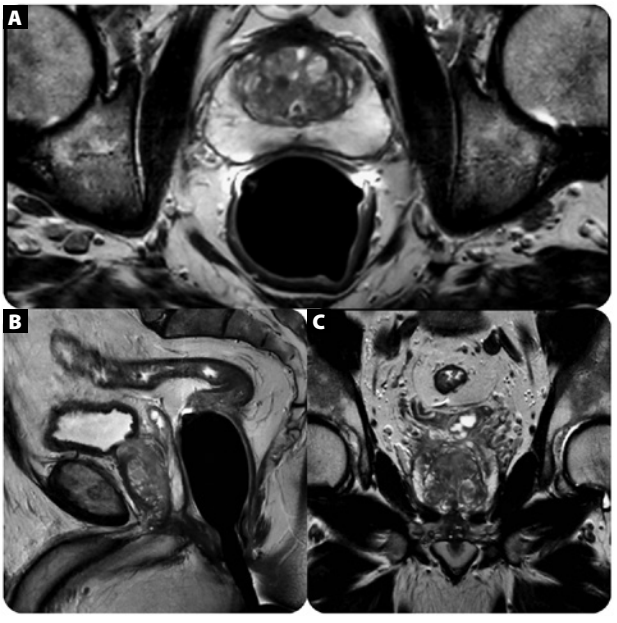

Figure 4. *T2-weighted axial (A), sagittal (B), and coronal (C) MR images of the prostate using the endorectal and torso coil. Images courtesy of the author.*

cannula and prepare for the injection of the gadolinium-based MR contrast agent.[11] Patients are led to the MR imaging room by the radiologist who will ask them to

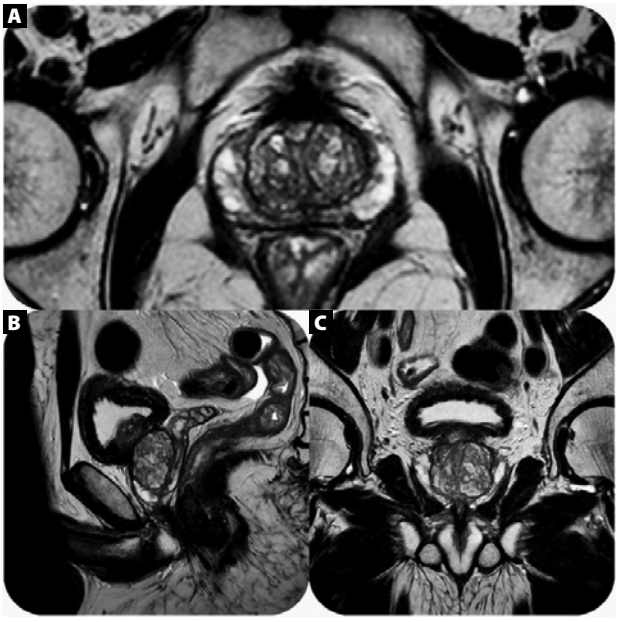

Figure 3. *T2-weighted axial (A), sagittal (B), and coronal (C) MR images of the prostate using the torso coil. Images courtesy of the author.*

lie supine with their arms along their body and a hearing protection device in place. A 32-channel cardiac phased-array coil will be placed on the anterior lower side of the abdomen; the centering always will be in the pubic symphysis area.

Examination Technique

A multiparametric MR imaging study of the prostate must follow the appropriate technique, which consists of T2 morphological sequences on 3 spatial planes and at least 2 functional sequences represented by DWI and dynamic contrast-enhanced MR imaging[12]; the latter is obtained after the injection of the contrast agent. The multiparametric MR imaging examination protocol developed at the author's center includes:

- morphological sequences – DWI $b = 0$ s/mm², 500 s/mm², 1000 s/mm², 1400 s/mm²; apparent diffusion coefficient map, 2000 s/mm² (para-axial plane with the same number of slices as the T2 sequences for a possible fusion of the images)
- MR spectroscopy (optional)

- T1 on the para-axial plane (optional) – delayed contrast enhancement on the para-axial plane during the injection of the MR contrast agent

When performing a morphological study, selecting the best result on spatial resolution and selecting thin layers and elevated matrix sizes associated with reduced field of view is important. Using the reduced field of view can cause the aliasing artifact along the phase encoding direction.[13] All the sequences are acquired with patients using a free-breathing technique.

The first acquisition plane is the sagittal plane in the sequence turbo spin-echo T2. This sequence will be placed on the localizer images while attempting to obtain an exact parallel orientation to the major axis of the prostate. The full acquisition must include the entire prostatic gland, the lateral seminal vesicles, and the bladder cranially. The main characteristics of the sequences usually acquired are:

- Para-axial plane of the elevated sequence and small field of view for obtaining a high resolution of the T2 plane; this is ideal for the identification for the zonal anatomy of the gland and for the visualization of the neurovascular bundle
- Submillimetrical matrix pixel size
- The sagittal and paracoronal planes are more suitable for the basal and apical regions of the gland and its relations to the surrounding structures.

The T2-weighted sequences on the para-axial plane are the most important from a diagnostic perspective because they highlight the presence of possible neoplastic lesions, which appear as hypointense areas and nodules that neatly contrast the high signal of the vascular component (see **Figure 5**). Parameters for this sequence are shown in the **Box**. In addition, the T2-weighted 3-D fast spin-echo sequences can integrate the conventional multiplanar and bidimensional (2-D) sequences; these 3-D sequences include 3-D VISTA (Philips Medical Systems), 3-D SPACE (Siemens Healthineers), and 3-D FSE-Cube (GE Healthcare).[14] These sequences use prolonged echo trains with variable flip angles to obtain high-resolution isotropic 3-D images (see **Figure 6**). The isotropic acquisition can be useful particularly for outlining small anatomical details and discerning real lesions from partial volume averaging.

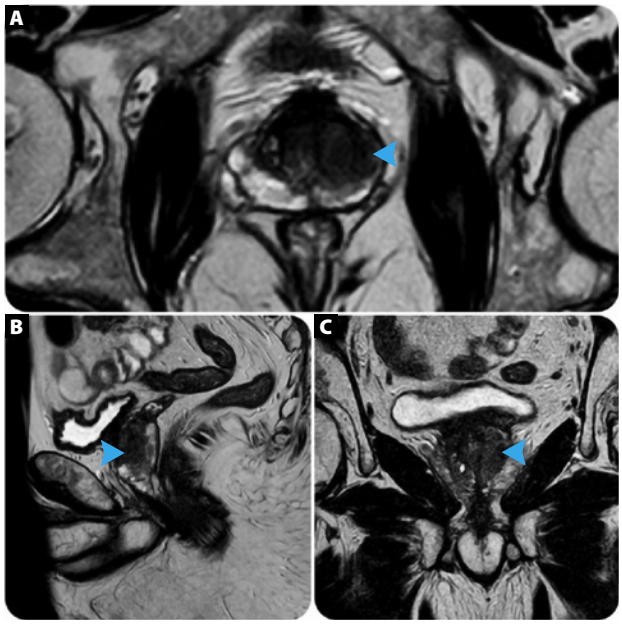

Figure 5. *T2-weighted axial (A), sagittal (B) , and coronal (C) MR images of the prostate with arrowheads indicating the lesion. Images courtesy of the author.*

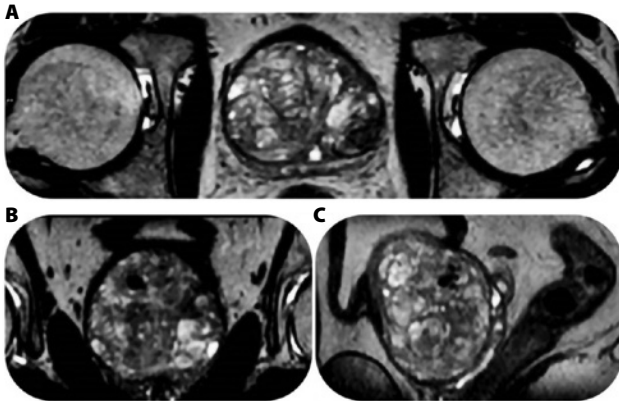

Figure 6. *Three-dimensional T2-weighted axial (A), reconstructed coronal (B), and reconstructed sagittal (C) MR images of the prostate. Images courtesy of the author.*

Eventually, the DWI sequences are carried out on the para-axial plane with the same inclination and number of slices as the T2-weighted sequences. The DWI is based on the molecular diffusion (ie, the temperature-inducted free movement of the molecules). The DWI are obtained with a modification of a T2 spin-echo

Box

Sequence parameters

Adequate coverage can be obtained with 20-30 slices of 3 mm in thickness with no slice gap. The echo time should be chosen to maximize the contrast between the peripheral and the transitional zone and between the neoplastic tissue and the gland tissue, based on their T2 intrinsic values. At 1.5 T, the T2 values of the neoplastic tissue of the transitional and peripheral zone are 82 ms, 88 ms, and 122 ms.

An echo time ranging from 100 to 130 ms typically is used to obtain an optimal contrast among these tissues with its repetition time between 2 and 5 seconds. The phase-encode direction should be set as left to right and the frequency encode direction as anterior to posterior to prevent the formation of ghosting artifacts, which are linked to rectal peristalsis and hide the prostate. A high spatial resolution is required to outline the prostate anatomy with precision and evaluate the infiltration of extra prostatic tissues.

echo-planar imaging sequence. Subsequently, diffusion sensitizing gradients are added together with a radiofrequency of 180°.

These gradients are at the core of DWI. Modifying their intensity results in a progressive decrease of the T2 weighting and an increase of the dependency of the signal intensity to the diffusion. The diffusion-weighted sequence, with different degrees of dependency, can be acquired from the diffusion signal, depending on the duration of the time between applications of varying *b* values. These parameters can be synthetized in the *b* value expressed as seconds per square millimeter (s/mm²). As the *b* value increases, the T2 weighting decreases and the diffusion weighting rises. DWI sequences are important because the tumor tissue tends to have minor diffusion compared with healthy tissue due to its high cellularity. In prostate tumors, the interstitial spaces and the gland lumens are substituted by tumor cells and fibrous stroma with a reduction of the free water movements, hence, the diffusion. Therefore, malignant tumor nodules appear as lesions in diffusion-weighted sequences with a high *b* value (see **Figure 7**). Calculating the apparent diffusion coefficient allows for quantifying the reduction of diffusivity (see **Figure 8**). Its value seems to be related to the Gleason score, or the index of tumor aggressiveness (see **Figure 9**).[9]

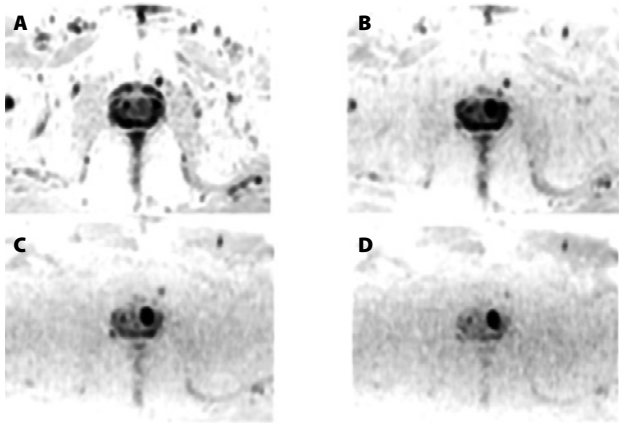

Figure 7. *Axial MR images (*b *values of 0 s/mm² [A], 500 s/mm² [B], 1000 s/mm² [C] 1400 s/mm² [D]) of a hypointense lesion. Images courtesy of author.*

The study continues with the perfusion sequences with delayed contrast enhancement before, during, and after the injection of MR contrast agent (0.1 mmol/kg or 0.2 ml/kg), with series perpendicular to the prostatic axis, maintaining the same conformation to obtain a combined evaluation of morphological and diffusion sequence. The aim of these sequences is to show the hypervascularization of the artery, which is typical of the most malignant tumor nodules, and to separate them from the healthy gland tissue.

The dynamic phases take at least 3 minutes from the injection of the agent with a 2 to 2.5 ml/s flow as initial injection, and this will be followed by more injections without breaks in between. The sequences are echo gradient with fat suppression.

In postprocessing, there are 3 different analyses: qualitative, semiquantitative, and quantitative. Qualitative analysis involves before and after contrast images without any quantification of the enhancement. The semiquantitative analysis is represented by radiographer-selected semiquantitative parameters, which are obtained from the time-intensity curve of the signal. They describe the evolution of the contrast-enhanced lesion, and at the author's facility, the protocol used is:

- onset time (timing of signal increase)
- enhancement peak (gap between maximum and base intensity)

- time peak (amount of time between onset time and enhancement peak)
- wash-in rate (the maximum slope between the time of onset of contrast inflow and the time of peak enhancement)
- washout rate (speed in which the enhancement falls after its peak)

Quantitative analysis is performed in few specialized facilities because of its long and complex software-run postprocessing phase. This analysis computes sophisticated pharmacokinetics parameters that outline microscopical processes regulating the contrast molecules' distribution in between the intra and extravascular space over time. In **Figure 10,** early impregnation of contrast area is shown. Positioning a region of interest on a lesion allows for an enhancement curve to be obtained that quantifies the intense and early enhancement common in a neoplastic nodule.

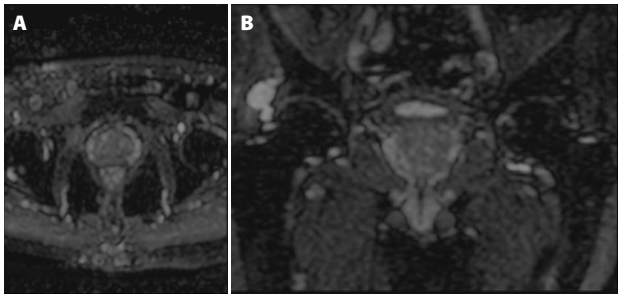

Figure 8. *Axial (A) and coronal (B) apparent diffusion coefficient. Images courtesy of the author.*

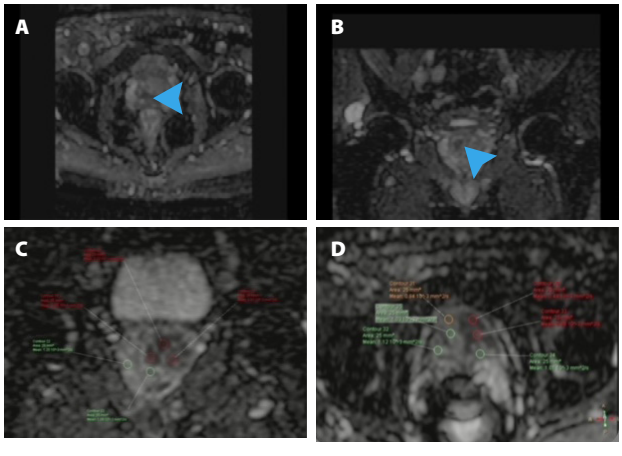

Figure 9. *Axial (A) (arrowheads indicate the lesion), coronal (B) (arrowheads indicate the lesion), coronal (C), and axial (D) quantify the cancerous lesion with the placement of different regions of interest. Images courtesy of the author.*

Magnetic Resonance Spectroscopy Imaging

MR spectroscopy imaging can identify the frequency of metabolites that usually are present in the glandular parenchyma in the peripheral area (high citrate content, low levels of choline and creatine) and in the transitional and midzone (reduced citrate content). In the carcinomatous tissue, the spectroscopic evaluation highlights high choline contents (3.2 ppm resonant frequency), which are due to the high turnover of the phospholipids in the cell membrane that is common in malignant processes, and a reduction in citrates (2.4 ppm resonant frequency) that tend to become oxidized. The inversion in the choline and citrate ratio in the neoplastic tissue is a parameter used to differentiate between healthy tissue and tumors of the prostate. The evaluation of the spectroscopic curve takes into consideration a suspicious voxel for the presence of neoplasia when the choline and creatine:citrate ratio is more than 2.[15]

Conclusion

Multiparametric MR imaging is an important tool in the detection of prostate tumors. It enables imaging

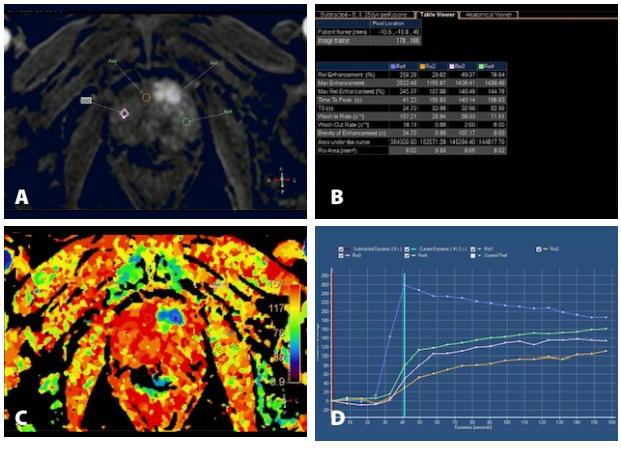

Figure 10. *Postprocessing dynamic contract enhanced MR images. Axial plane with 4 regions of interest positioned (A), table viewer (B), axial plane colored map of quantification (C), and peak improvement graph (D). Images courtesy of the author.*

of different zones of the gland and suspected neoplasia. In addition, it is a method that offers prognostic in vivo information that can improve outcomes for patients.

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A heartfelt thanks to Dr Carmelo Tuscano, of the Radiation Oncology Department at Grand Metropolitan Hospital, for reviewing the manuscript.

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