Magnetic resonance imaging and prostate cancer: a brief timeline

Ressonância magnética e câncer de próstata: uma breve história no tempo

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The English speaking authors often refer to prostate cancer as an elusive disease. Although the literal translation of elusive to our Portuguese language is closer to the English word cunning, perhaps the Portuguese expression that best adapts to the context is "algo difícil de compreender"[1], which literally means, something difficult to understand. And, undoubtedly, so is prostate cancer.

For more than 30 years, the combination of digital rectal examination and the prostate specific antigen (PSA) test has been utilized in the screening for prostate cancer, and prostate biopsy guided by transrectal ultrasonography (US) has been established as a necessary and sufficient method for histological confirmation of the disease. Despite the limitations of these diagnostic methods (such as the prevalence of up to 27% of tumors in patients with PSA below the 4 ng/ml cut-off limit), there is evidence that they will remain in use for years to come[2]. On the other hand, if the prostate cancer diagnosis seems to be problematic in principle, it is from confirmation of the diagnosis that the biggest problems really begin (both for the patient and the physicians).

An array of clinical, laboratory and imaging and methods, may be employed for staging the disease, from the urologist expertise in locally staging the lesion by means of digital rectal examination, then on to clinical nomograms (with Partin and Kattan being the most known ones) and peaking with sometimes confusing requests for anatomic and functional imaging methods, such as Doppler US, abdominal and pelvic computed tomography (CT), total abdomen magnetic resonance imaging (MRI), bone scintigraphy and positron emission tomography – helical computed tomography (PET-CT). To further complicate this equation, even though radical prostatectomy remains as the main therapeutic option, there is no consensus with respect to the ideal treatment in several clinical situations, with the options of external radiotherapy, brachytherapy, hormonal blockade and active vigilance. Moreover, one should remember that radical prostatectomy is not the only method, as there are the options of open surgery, laparoscopic or robotic surgeries.

This lack of consensus on the diagnosis- staging-treatment algorithm leads to exaggerated and often mistaken requests for imaging studies, making the patient global evaluation much more expensive. Requests for bone scintigraphy for investigating the presence of distant metastases in patients with prostate tumors confirmed by biopsy are not uncommon, although it is widely known that this study will present positive results for less than 5% of patients with < 20 ng/ml PSA level[3]. Likewise, total abdomen CT requested for this same patients subgroup will identify lymphadenopathies in only 1% of the cases[4]. In other words, a lot of time, money and ionizing radiation are spent, with no actual benefit to the greatest majority of patients.

The advent of endorectal coil magnetic resonance imaging (MRI) in the early nineties of the last century seemed to be a light at the end of the tunnel. Good spatial resolution, exceptional contrast-resolution, no radiation..., everything to make it a breakthrough. Initially, however, it really was not so. The first results in local staging were so disappointing (sensitivity and accuracy of approximately 50% in some studies, reminding us of the depreciative analogy of tossing a coin), that an article published by the respected **Journal of Urology** clearly stated at its conclusion: "We advise

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against routine use of this imaging modality in staging clinically localized cancer"[5]. End of the game? Not yet.

Fortunately, there were persevering radiologists in those times. They advocated the standardization of minimum requirements for the performance of the study (1.5 tesla equipment, T2-weighted FSE sequences with high spatial resolution, utilization of antiperistaltic drugs, and minimum three-week interval between the biopsy and the MRI study), and the definition of more specific criteria of extra-prostatic tumor extent, making it possible to obtain satisfactory and reproducible results in local neoplastic staging. In a short time, the results improved significantly, reaching specificities of more than 85% in the determination of extracapsular extent and seminal vesicle invasion[6] . However, one problem still remained: the tumor detection in the peripheral region of the prostate is based on the identification of areas with low signal intensity on T2-weighted sequences, which are non-specific, possibly representing various other types of lesions (such as hemorrhage, prostatitis, trauma sequels, fibrosis, and so on). How is it possible to increase the specificity in tumors detection, thus improving the method accuracy in local staging? Instead of one single answer, we actually have three: spectroscopy, perfusion and diffusion.

Spectroscopy, whose principle is based on the identification of suspected areas by the analysis of relative endogenous metabolites concentration present in healthy and neoplastic prostate tissues, received widespread attention as if it were a panacea, and as it often happens with such things, it almost had a short life. A lot of persistence from radiology professionals was necessary to establish the actual applicability of the method with its advantages and limitations. On its turn, gadolinium-enhanced dynamic perfusion imaging is aimed at detecting suspect areas based on hemodynamic differences between the tumor and the adjacent prostatic tissue. Finally, not long ago, there has been an upsurge in the use of diffusion-weighted sequences to identify neoplastic tissue foci. These three complementary techniques, utilized separately or in association, received a lot of attention in the uroradiological literature over the last ten years, and have contributed to establish endorectal MRI as the best method for locoregional staging of prostate cancer (for the more skeptic ones, I recommend reading three articles published in **Radiology** by the interdisciplinary group from Memorial Sloan-Kettering Cancer Center between 2004 and 2007, demonstrating that MRI spectroscopy did better than all clinical-laboratory predictive models available for neoplastic local staging)[7–9].

Let us focus, then, on the novel and potentially promising MRI applications on prostate cancer. The first one is the previous detection of suspicious areas in patients with negative biopsies, and persistent clinical suspicion of neoplasm (high PSA level and/or altered digital rectal examination) to guide in the collection of additional fragments of such regions in a new US-guided biopsy, thus increasing the biopsy sensitivity in cancer detection. Although some studies report sensitivity in the order of 90% in the identification of prostate tumors through MRI spectroscopy or MRI perfusion, the reality of studies approaching tumor detection in patients with clinical suspicion previous to rebiopsy, was a little different: accuracy ranging from 65% to 80%, and positive predictive value ranging between 58% and 75%[10,11]. This goes without mentioning the increase cost incurred with the large scale utilization of this method and the trouble caused by the use of endorectal coils in patients without a confirmed neoplastic diagnosis. Promising? Yes. Widely recommendable? Not yet.

The 3 tesla MRI, already available in several centers in Brazil, certainly deserves to be mentioned. The signal gain provided by the larger magnetic field makes it possible to acquire images without the necessity of endorectal coils, with spatial resolution similar to that of 1.5 tesla MRI with such coils. If by on hand the real applicability of such technique in local staging still remains to be confirmed by further studies, on the other hand there are certainly great prospects for the application of this method in prebiopsy detection of tumor in patients with persistent clinical suspicion of neoplasm (sparing the patient of the trouble and discomfort with the endorectal coil insertion). And there is also the option of performing local staging in the 3 tesla equipment with endorectal coil, generating images with even higher spatial resolution.

The study developed by Melo et al. included in the present issue of **Radiologia Brasileira**, brings to light a real problem faced by a large number of centers that choose to perform prostatic MRI: the establishment of a standardization of the study and of a learning curve, to allow the achievement of similar (or better) results than those reported by the literature. A difficult, but absolutely necessary task [12].

Finally, a challenge: what will be the greatest revolution in imaging evaluation of prostate cancer? There

are some who prospect the commercial availability of lymphotropic superparamagnetic contrast agent based on iron nanoparticles which promise a complete change in paradigm in lymph-node staging in cases of prostate cancer (accuracy > 95%!)[13].

Others, prospect on the improvement of MRI sequences capable of differentiating aggressive tumors (that deserve therapy with curative intent) from those that are actually non significant (that may be followed up by means of active vigilance)[14].

Make your bets.

REFERENCES

1. Michaelis Moderno dicionário inglês – inglês-português/português-inglês. São Paulo: Melhoramentos; 2007.
2. Thompson IM, Pauler DK, Goodman PJ, et al. Prevalence of prostate cancer among men with a prostate-specific antigen level < or =4.0 ng per milliliter. N Engl J Med. 2004;350:2239–46.
3. Abuzallouf S, Dayes I, Lukka H. Baseline staging of newly diagnosed prostate cancer: a summary of the literature. J Urol. 2004;171(6 Pt 1):2122–7.
4. Huncharek M, Muscat J. Serum prostate-specific antigen as a predictor of staging abdominal/pelvic computed tomography in newly diagnosed prostate cancer. Abdom Imaging. 1996;21: 364–7.
5. Perrotti M, Kaufman RP Jr, Jennings TA, et al. Endo-rectal coil magnetic resonance imaging in clinically localized prostate cancer: is it accurate? J Urol. 1996;156:106–9.
6. Cornud F, Belin X, Flam T, et al. Local staging of prostate cancer by endorectal MRI using fast spin-echo sequences: prospective correlation with pathological findings after radical prostatectomy. Br J Urol. 1996;77:843–50.
7. Wang L, Mullerad M, Chen HN, et al. Prostate cancer: incremental value of endorectal MR imaging findings for prediction of extracapsular extension. Radiology. 2004;232:133–9.
8. Wang L, Hricak H, Kattan MW, et al. Prediction of organ-confined prostate cancer: incremental value of MR imaging and MR spectroscopic imaging to staging nomograms. Radiology. 2006;238:597–603.
9. Wang L, Hricak H, Kattan MW, et al. Prediction of seminal vesicle invasion in prostate cancer: incremental value of adding endorectal MR imaging to the Kattan nomogram. Radiology. 2007;242:182–8.
10. Prando A, Kurhanewicz J, Borges AP, et al. Prostatic biopsy directed with endorectal MR spectroscopic imaging findings in patients with elevated prostate specific antigen levels and prior negative biopsy findings: early experience. Radiology. 2005;236:903–10.
11. Yuen JS, Thng CH, Tan PH, et al. Endorectal magnetic resonance imaging and spectroscopy for the detection of tumor foci in men with prior negative transrectal ultrasound prostate biopsy. J Urol. 2004;171:1482–6.
12. Melo HJF, Szejnfeld D, Paiva CS, et al. Espectroscopia por ressonância magnética no diagnóstico do câncer de próstata: experiência inicial. Radiol Bras. 2008;42:1–6.
13. Harisinghani MG, Barentsz J, Hahn PF, et al. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. N Engl J Med. 2003;348:2491–9.
14. Shukla-Dave A, Hricak H, Kattan MW, et al. The utility of magnetic resonance imaging and spectroscopy for predicting insignificant prostate cancer: an initial analysis. BJU Int. 2007; 99:786–93.