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Review

Reprint of "Update on ultrasound elastography: Miscellanea. Prostate, testicle, musculo-skeletal"☆

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ABSTRACT

Nowadays ultrasound elastosonography is an established technique, although with limited clinical application, used to assess tissue stiffness, which is a parameter that in most cases is associated with malignancy.

However, although a consistent number of articles have been published about several applications of elastosonography, its use in certain human body districts is still not well defined.

In this paper we write on the use of elastosonography in prostate, testicle and musculo-skeletal apparatus. We report and compare the work of several authors, different type of elastosonography (shear wave, strain elastography, etc.) and instrumental data obtained in the study of both benign and malignant lesions.

1. Introduction

When a single examination cannot solve a diagnostic problem, it is usually correct to request cross sectional imaging to achieve an accurate diagnosis. Over time, grey-scale ultrasound equipment has been improved with colour Doppler, power Doppler, software for contrast enhanced studies and more recently also elastography, which is performed for various diagnostic purposes.

However, elastography is still a tool with limited clinical application. We therefore decided to add a chapter called 'miscellaneous' and include elastography which is still not regularly used in prostate, testicle and musculo-skeletal disorders.

2. Prostate

2.1. Introduction

Prostate cancer is a public health issue, because it is the cancer with the highest incidence rate and the second cause of cancer death in men. In addition, prostate cancer is the most commonly diagnosed malignancy in men (besides skin cancer) with an estimated 790,000 cases in 2012 and 217,730 new cases diagnosed every year in the USA. Despite improvement in diagnosis and therapy, the specific mortality rate started to fall since 2000.

2.1.1. Prostate cancer screening

There is no systematic screening in most European countries and United States due to the lack of an effective and simple test to pinpoint men with a risk of cancer high enough to justify continuing the diagnostic procedure with more aggressive tests. For over 30 years, the individual screening for prostate abnormalities has been the combination of digital rectal examination (DRE) and prostate specific antigen (PSA) test for men over 50 without predisposition and after disclosing the benefits and risks of over diagnosis. An abnormal or rising serum PSA level, or an abnormal digital rectal examination, triggers further evaluation, typically with transrectal ultrasound (TRUS)-guided sextant biopsies. Prostate biopsy findings are used to estimate the tumour volume (number of positive samples and length of tumour invasion) and aggressiveness

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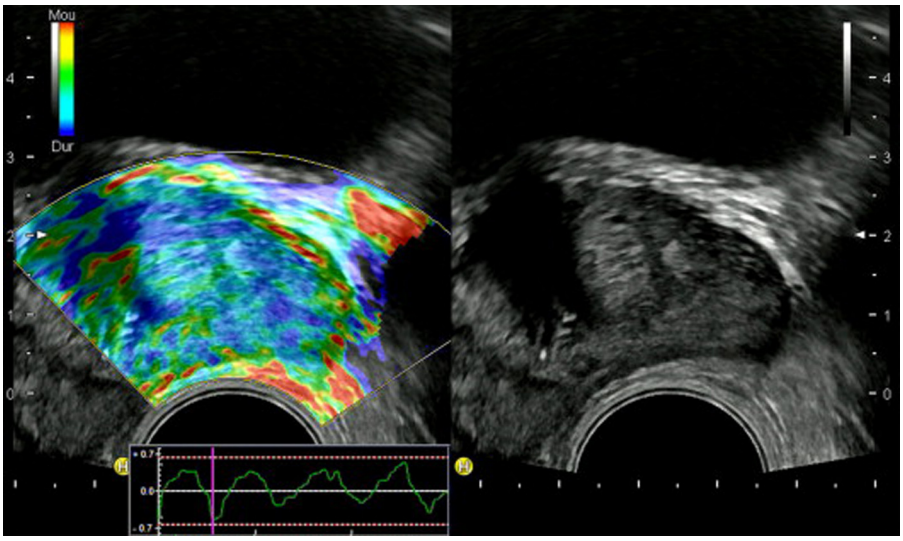

Fig. 1. Strain elastography: the transducer is used as a compression device and applies alternative cycles of compression and relaxation. A speckle comparison, before and after compression, yields to a colour map of local tissue deformation or strain called elastogram.

(Gleason score). Due to the dramatic increasing incidence provided by PSA screening and the short mortality reduction, the 5-year survival rate drastically increased by almost 30% in a 25 years, reaching 98% [1]. However, increase of PSA is not specific of prostate cancer and can be related to prostatic hyperplasia, acute and chronic prostatitis, or prostate trauma (caused by cystoscopy, resection, and biopsies). Moreover, there are significant prostate cancers with PSA levels lower than the threshold of 4 ng/ml.

2.1.2. Prostate cancer diagnosis

The diagnostic tools for prostate cancer diagnosis exhibit some strong limitations. PSA screening leads to a substantial number of unnecessary biopsies in patients with no cancer or with indolent cancer that do not need immediate treatment, with an estimated over-detection rate ranging from 27% to 56% [2]. The false negative rate of prostate biopsy varies from 17% to 21%, in patients with a negative first series of biopsies [3]. The increase in the number of core biopsies improves prostate cancer detection and offers a better estimation of the tumour volume and Gleason score, but even saturation biopsies cannot rule out prostate cancer. It has many limitations including increased cost, morbidity and over diagnosis of microscopic tumour foci [4,5]. Many urologists are now facing a dilemma when patients present with an abnormal level of PSA and negative biopsies: when should one stop and when should one continue carrying out biopsies [4].

Multi-parametric MRI (MP-MRI) combines T2-weighted imaging with functional sequences such as diffusion sequence (including ADC calculation), dynamic contrast-enhanced sequence and spectro-MRI. It has become a major modality for tumour detection and staging [6,7], particularly in candidates to radical prostatectomy [8,9]. However, MRI performance varies depending on which combination of positive features is selected for cancer diagnosis between T2-weighted sequence, diffusion sequence and dynamic contrast-enhanced sequence [10]. If the sensitivity of MP-MRI is high its specificity remains low especially because it is affected by the hypervascularity of the normal inner gland and coexisting benign prostatic hyperplasia (BPH) nodules. Its performance remains low for the detection of small lesions of limited Gleason score ($\leq$6) and there is little information to help distinguish between aggressive and indolent tumours. Additional limitations include cost, limited availability, contra-indication to MRI and contrast agents, and the fact that the very large majority of biopsies are ultrasound guided.

Conventional TRUS B-mode imaging is known for its limited sensitivity and specificity in between 40% and 50% for prostate cancer detection, and not significantly improved by colour/power Doppler [11]. Contrast-enhanced ultrasound is still under evaluation and can sensitize prostate biopsy [12,13]. However, the contrast ratio between the cancer and the normal peripheral zone is highly transient (a few seconds).

Prostate TRUS elastography has been developed in order to identify stiff tissues, identified during DRE as prostate cancer is stiffer than normal prostate tissue [14–25]. They are 2 different approaches, the quasi-static (or strain) elastography that was introduced more than 10 years ago [14–17], and the shear wave elastography that became available for prostate examination 3 years ago [18–20]. These techniques are intrinsically limited to stiff cancer, taking into account that all stiff lesions are not cancers.

2.1.3. Technical background and examination procedure

2.1.3.1. Quasi-static/strain elastography (SE). Soft tissues tend to exhibit higher strain (deformation) than stiffer areas when compression is applied, and strain is linked to the stiffness represented by the Young's modulus E by the following equation, where σ is the stress applied to the tissue and ε is the resulting strain:

$$E = \frac{\sigma}{\varepsilon}$$

Quasi-static ultrasound elastography (or strain elastography, SE) of the prostate is based on the analysis of tissue deformation in a region, generated by inducing a mechanical stress (tissue compression by the transrectal transducer itself); the deformation is then supposed to be uniform in space and intensity. For prostate elastography, the external stress is applied on the patient rectal wall adjacent to the prostate peripheral zone, by using the transrectal transducer as a compression device (Fig. 1). A water filled balloon between the imaging probe and the rectal wall can be used to improve the homogeneity of the deformation [11]. A speckle comparison, before and after compression, yields to a colour map of local tissue deformation or strain called elastogram. The tissue stiffness is estimated by visualizing the differences in strain between adjacent regions. Therefore no quantitative elasticity analysis is available. The stiffness colour scale is automatically distributed from the lowest to the highest strain found in the stiffness box or region-of-interest (ROI), this is why the size and position of the stiffness box may induce artefactual variation of the displayed strain.