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Multiparametric Magnetic Resonance Imaging and Magnetic Resonance Imaging Fusion-Guided Biopsy for the Diagnosis of Prostate Cancer: Current Status

Valentina Testini^{1,2}, Laura Eusebi³, Francesco Saverio Guerra¹, Willy Giannubilo⁴, Manuel Di Biase⁵, Annunziata Russo², Giuseppe Guglielmi^{1,2,6}

¹ Foggia University, Foggia, Italy;

² Monsignor Raffaele Dimiccoli, Barletta, Italy;

³ Carlo Urbani Hospital, Jesi, Italy;

⁴ Ospedale Civile, Civitanova Marche, Italy;

⁵ Santa Maria della Misericordia Hospital, Perugia, Italy;

⁶ Casa Sollievo della Sofferenza Hospital, Foggia, Italy

ABSTRACT

This review explains the role of multiparametric magnetic resonance imaging, particularly in prostate biopsy, in the detection of prostate cancer. The use of multiparametric magnetic resonance imaging in the diagnosis of prostate cancer has also allowed its use in magnetic resonance imaging-guided biopsies, which according to many studies present high sensitivity and specificity in early diagnosis and staging, in patients with persistently high prostate-specific antigen levels despite previous negative prostate biopsies, and in the follow-up of patients under active surveillance.

To perform a targeted prostate biopsy, three types of magnetic resonance imaging guidance are available: cognitive fusion, direct magnetic resonance imaging-guided biopsy performed within a tomograph (in-bore biopsies), and software coregistration of stored magnetic resonance images with real-time ultrasound using a fusion device, with multiparametric magnetic resonance imaging findings digitally overlaid on real-time transrectal ultrasound images for targeted biopsy.

Each method has its advantages and disadvantages. Magnetic resonance imaging-targeted biopsy improves the quality of histological results compared with other approaches, with approximately 90% correct detection of significant index lesions. Correct staging allows the selection of the best therapeutic options, adequate evaluation of the prognosis, and reduction of the incidence of new biopsies and complications. The current objective is to make magnetic resonance imaging-guided biopsy increasingly available and standardize the technique to minimize inter-operator variability depending on the available system.

Keywords: multiparametric magnetic resonance imaging; prostate cancer; fusion biopsy; targeted biopsy.

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Возможности мультипараметрической магнитно-резонансной томографии при проведении фьюжн-биопсии под её контролем в диагностике рака предстательной железы: текущий статус

V. Testini^{1,2}, L. Eusebi³, F.S. Guerra¹, W. Giannubilo⁴, M. Di Biase⁵, A. Russo², G. Guglielmi^{1,2,6}¹ Университет Фоджи, Фоджа, Италия;² Monsignor Raffaele Dimiccoli Hospital, Барлетта, Италия;³ Carlo Urbani Hospital, Ези, Италия;⁴ Ospedale Civile, Чивитанова-Марке, Италия;⁵ Santa Maria della Misericordia Hospital, Перуджа, Италия;⁶ Casa Sollievo della Sofferenza Hospital, Фоджа, Италия

АННОТАЦИЯ

В данном обзоре освещается роль мультипараметрической магнитно-резонансной томографии в выявлении рака предстательной железы, в частности — при биопсии простаты. Использование мультипараметрической магнитно-резонансной томографии в диагностике рака простаты позволяет также применять её для биопсии. Мультипараметрическая магнитно-резонансная томография, по данным многих исследований, обладает высокой чувствительностью и специфичностью в ранней диагностике и стадировании у пациентов с сохраняющимся высоким уровнем простатспецифического антигена, несмотря на предыдущие отрицательные биопсии простаты, а также при ведении пациентов, находящихся под активным наблюдением.

Для проведения прицельной биопсии простаты существует три типа наведения: когнитивная фьюжн-биопсия; прямая биопсия, направляемая магнитно-резонансной томографией и выполняемая внутри томографа (in-bore); программная корегистрация снимков предоперационной магнитно-резонансной томографии с интраоперационным ультразвуковым исследованием с помощью фьюжн-устройства. При этом при проведении прицельной биопсии результаты мультипараметрической магнитно-резонансной томографии накладываются в цифровом виде на изображения трансректального ультразвукового исследования в реальном времени.

Каждый метод имеет свои преимущества и недостатки. Прицельная биопсия с помощью магнитно-резонансной томографии улучшает качество гистологических результатов по сравнению с другими подходами, выявляя значимые индексные поражения с точностью до 90%. Правильное стадирование позволяет выбрать оптимальные варианты лечения, адекватно оценить прогноз, снизить частоту новых биопсий и осложнений. В настоящее время главная задача состоит в том, чтобы сделать биопсию в сочетании с магнитно-резонансной томографией более доступной и стандартизировать технику проведения процедуры, что позволит минимизировать межоператорскую вариабельность в зависимости от используемой системы.

Ключевые слова: мультипараметрическая магнитно-резонансная томография; рак предстательной железы; фьюжн-биопсия; прицельная биопсия.

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融合引导活检在前列腺癌诊断中的多参数磁共振成像功能：现状

Valentina Testini^{1,2}, Laura Eusebi³, Francesco Saverio Guerra¹, Willy Giannubilo⁴,
Manuel Di Biase⁵, Annunziata Russo², Giuseppe Guglielmi^{1,2,6}

¹ Foggia University, Foggia, Italy;

² Monsignor Raffaele Dimiccoli, Barletta, Italy;

³ Carlo Urbani Hospital, Jesi, Italy;

⁴ Ospedale Civile, Civitanova Marche, Italy;

⁵ Santa Maria della Misericordia Hospital, Perugia, Italy;

⁶ Casa Sollievo della Sofferenza Hospital, Foggia, Italy

摘要

本综述强调了多参数磁共振成像在前列腺癌检测中的作用，特别是在前列腺活检中的作用。多参数磁共振成像技术在前列腺癌诊断中的应用也可用于活检。许多研究报告称，多参数磁共振成像在前列腺活检阴性但前列腺特异性抗原水平持续偏高的患者的早期诊断和分期方面具有很高的灵敏度和特异性，在主动监测患者的管理方面也是如此。

前列腺靶向活检有三种引导方式：认知融合引导活检；由磁共振成像引导并在计算机断层扫描仪内（in-bore）进行的直接活检；以及使用融合设备对术前磁共振成像图像和术中超声检查进行的软件联合注册。在这种靶向活检中，多参数磁共振成像结果以数字方式叠加在实时经直肠超声图像上。

每种方法都有其优缺点。与其他方法相比，利用磁共振成像进行靶向活检可提高组织学结果的质量，检测重要指标病变的准确率高达 90%。正确的分期可以选择最佳治疗方案，充分评估预后，减少新的活检和并发症的发生。目前的主要任务是使活检与磁共振成像相结合的应用更加广泛，并使手术技术标准化，以最大限度地减少因所使用的系统不同而造成的操作者之间的差异。

关键词：多参数磁共振成像；前列腺癌；融合引导活检；靶向活检。

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INTRODUCTION

In Western countries, prostate cancer (PCa) is the most frequent noncutaneous tumor in men [1]. According to the European Association of Urology (EAU) recommendations, prostate biopsy is the gold standard for PCa diagnosis.

The first diagnostic biopsy method is the random technique (rather than sextant), with 12 samples taken only in the peripheral zone [2]. This technique has limitations such as undersampling (insufficient number of samples in relation to the prostate volume), oversampling (excessive core number, with identification of the nonsignificant microfoci), overstaging, with a diagnosis of nonsignificant tumors (low sensitivity), understaging, with failure to diagnose clinically significant cancers (low specificity), and operator experience-related errors [3].

The new therapeutic trend of active surveillance (AS; for low-risk tumors and minimally invasive targeted procedures necessitates more precision in prostate examination, necessitating advancements in the biopsy approach.

Prostate biopsy is currently recommended for men aged 50–69 years with high serum prostate-specific antigen (PSA) levels (>3 ng/mL) or abnormal digital rectal examination findings (nodules, induration, and asymmetry). After the first set of negative biopsy results, when suspicion of PCa remains high, the number of samples (i.e., saturation biopsy) and sampling of the transitional zone should be increased [4].

Since its initial application in 1983, MRI has been widely used for PCa diagnosis because of its increased availability and multiparametric imaging, which combines anatomical and functional data [5, 6].

In 2012, the European Society of Urogenital Radiology published guidelines based on expert consensus to standardize the evaluation and reporting of prostate MRI: the Prostate Imaging Reporting and Data System (Pirads) [7]. Since then, the Pirads score has been externally evaluated and found to be reliable for more accurate PCa detection [8].

In 2019, the Pirads Steering Committee published updated reporting guidelines describing the assessment categories and technical parameters described in version 2 of the Pirads [9].

With these premises, the role of multiparametric MRI (mpMRI) has become central not only in the diagnosis of PCa but also in biopsy as a tool for correct staging and assessment of tumor extension (Gleason score [GS]).

The current goal is to make MR-guided biopsy increasingly available, thereby minimizing interoperator variability depending on the available system.

METHODS OF MAGNETIC RESONANCE IMAGING GUIDED PROSTATE BIOPSY

To perform a targeted prostate biopsy, three types of MRI guidance are available:

- Cognitive fusion, in which the operator visually directs the transrectal ultrasound (TRUS)-guided biopsy to the prostate area of abnormalities on mpMRI.
- Direct MRI-guided biopsy, performed within an MRI tube (in-bore biopsies): This technique is quite precise for identifying areas of interest within the prostate; however, it is time-consuming, expensive, and impractical because the entire process is performed within the MRI gantry [10].
- Software coregistration of stored MRI with real-time US using a fusion device, with mpMRI findings digitally overlaid on real-time TRUS images for targeted biopsy (TB). This procedure can be performed using elastic fusion systems (e.g., Koelis Urostation and Eigen Artemis) or rigid fusion systems (e.g., Philips Uronav, Eindhoven, The Netherlands; Medcom BiopSee, Darmstadt, Germany).

Each method has its advantages and disadvantages.

Despite substantial variation in the sensitivity of detecting clinically indolent disease across studies, most studies have shown that the sensitivity of MR–US fusion (cognitive or device) ranges between 80% and 95% [11].

The main clinical indications for MR–US fusion biopsy are persistently high PSA levels despite previous negative prostate biopsies and follow-up of patients on AS [12].

Cognitive Fusion

Cognitive fusion is performed easily and rapidly and does not require any additional equipment other than an MRI and a standard TRUS facility. The US operator does not need any additional training beyond the standard TRUS-guided biopsy. Cognitive fusion is based on the sonographer's ability to localize the region of interest by imaging its location within the prostate after viewing the worrisome lesion on MRI [12].

MRI and TRUS images are superimposed by a cognitive overlay during biopsy, which can be performed with a printed document or by presenting MR images on the screen of a workstation in the TRUS room adjacent to the TRUS platform [13].

The physician aims at the target lesion with knowledge of lesion localization on MRI. The advantages of cognitive fusion are speed and simplicity; that is, it does not require additional equipment beyond what is ordinarily necessary for a TRUS-guided biopsy [14].

However, one of the downsides of cognitive fusion biopsy approaches is the possibility of sampling error when attempting to conceptualize the region of interest, which is particularly problematic for smaller tumors. Another disadvantage is the inability to track the position of each previous biopsy.

Despite this, the tumor detection rate of cognitive fusion is comparable to that of device-mediated fusion, and in most investigations, both cognitive and device-mediated fusions appear to be superior to random systematic sampling alone [15,16].

The disadvantage of cognitive fusion is the possibility of human error in extrapolating from MRI to TRUS in the absence of a real overlay.

Several studies have assessed the value of cognitively performed TB. Lawrentschuk et al. found that cognitive TB performed better than random cores, particularly in anterior lesions [17]. In a retrospective analysis, Haffner et al. compared TB results with those of 12 random biopsies in 555 patients [18]. A TB approach alone would have required just 3.8 cores per patient, thereby avoiding unnecessary biopsies in 38% of patients with normal MRI findings and avoiding the detection of minor cancer discovered by random biopsies in 13% of cases [18].

In this study, 13 significant cancers were missed with TB alone, whereas 12 significant cancers were missed with the standard approach [18].

In another study, Puech et al. discovered that MRI before biopsy increased the cancer detection rate (CDR) from 59% by 12-core saturation biopsy (SB) to 65% by cognitive TB [15].

In terms of significant cancer (cancer core length > 3 mm on any core and GS > 3 + 3), the CDRs were 67% for TB and 52% for conventional biopsies [15].

Labanaris et al. demonstrated that TB allowed for a 90% match between biopsy and surgical GS and indicated that MRI should be performed before biopsy to decrease SB underestimation of GS [19].

Thus, current research suggests that MRI-guided biopsy has higher accuracy and CDRs than standard TRUS-guided biopsy.

Haffner et al. reported that cognitive fusion is no better than systematic biopsies in men with questionable MRIs, highlighting the major risk associated with cognitive fusion: interobserver variability [18]. Although the present literature on cognitive fusion shows potential in the hands of professional cognitive fusionists, most urologists are now shifting toward commercially accessible device-mediated platforms because of the lack of tracking and digital overlay.

Direct Magnetic Resonance Imaging Guided Biopsy is Performed 'In-Bore'

A radiologist performs direct MRI-guided biopsy "in-bore," that is, within the MRI tube, by fusing a previous MR image indicating a lesion with a contemporaneous MR image to confirm biopsy needle localization. The transrectal route is employed. After each biopsy sample, the patient is scanned to ensure localization. Typically, only a few targeted cores are taken, and systematic sampling is not conducted.

The in-bore biopsy method provides the benefits of precision needle placement, fewer sampled cores, and a low risk of missed targets if they are visible by MRI [20]. Its disadvantages include greater expense and time consumption and the inability to regularly sample the residual gland [20]. This is relevant because MRI misses approximately 10% of severe lesions compared with final RP pathology [21,22].

Quentin et al. showed that in-bore TB has an excellent significant CDR of 92.2% [23]. Hoeks et al. reported that 265 patients with dubious lesions on mpMRI who had

previously negative TRUS biopsies had transrectal in-bore TB, resulting in a CDR of 41%, with 87% of the identified tumors being clinically significant [24].

The Barentsz group at Radboud University in Nijmegen, The Netherlands, presented a vast experience with in-bore biopsy [25]. The benefits of this procedure include a reduced number of cores taken, precise localization of the biopsy, and less detection of insignificant tumors. The downsides of this procedure include the time and cost, including the in-bore time, and two MRI sessions are required to obtain the biopsy specimens.

Furthermore, because only suspicious lesions are sampled, tissues with a "normal" MRI appearance are not collected, which is problematic because any false-negative characteristics of prostate MRI are unknown [25].

Fusion of Magnetic Resonance Imaging and Transrectal Ultrasound

In this method, the operator images the prostate using US, as has been used for decades. While viewing the prostate, the MR images of that prostate, in which imaging was performed beforehand and images were stored in the device, are fused with real-time US images using a digital overlay, allowing the target(s) previously delineated by a radiologist to be brought into the US machine's aiming mechanism. Fusion produces a three-dimensional (3D) reconstruction of the prostate, and the aiming and tracking of biopsy sites occur on the reconstructed model (Fig. 1 and 2) [25]. Several commercial platforms are now available, each with a different method of coregistration and a different hardware platform for lining up the biopsy with the coregistered picture [3]. Compared with VE, MRI-TRUS fusion-guided biopsy may have higher reproducibility because of less operator dependence and delivery of real-time feedback on actual biopsied areas [3]. The disadvantages include higher software/device costs, dependence on software for accuracy, and the associated learning curve and operator training [26] (Fig. 3 and 4).

This method has the disadvantage of being an indirect method, requiring the use of an additional device, and requiring specialized operator training. The benefit is that it may be performed in minutes in an outpatient clinic environment under local anesthesia, using techniques that have been used for years. The results obtained using the fusion device are highly encouraging [25].

Device-mediated fusion allows for the targeting of biopsies into previously defined MRI regions of interest using a 3D rendering apparatus that superimposes saved MR images on real-time US images, a technique known as coregistration. Although several commercial MR-US fusion platforms are available, all use some types of image coregistration and needle/probe tracking (mechanical or electromagnetic). These technologies enable the acquisition, storage, and reconstruction of real-time US images and the creation of 3D maps of lesion locations and prior biopsy sites for future reference [27]. Because any movement of the patient or the prostate affects image coregistration, these fusion devices

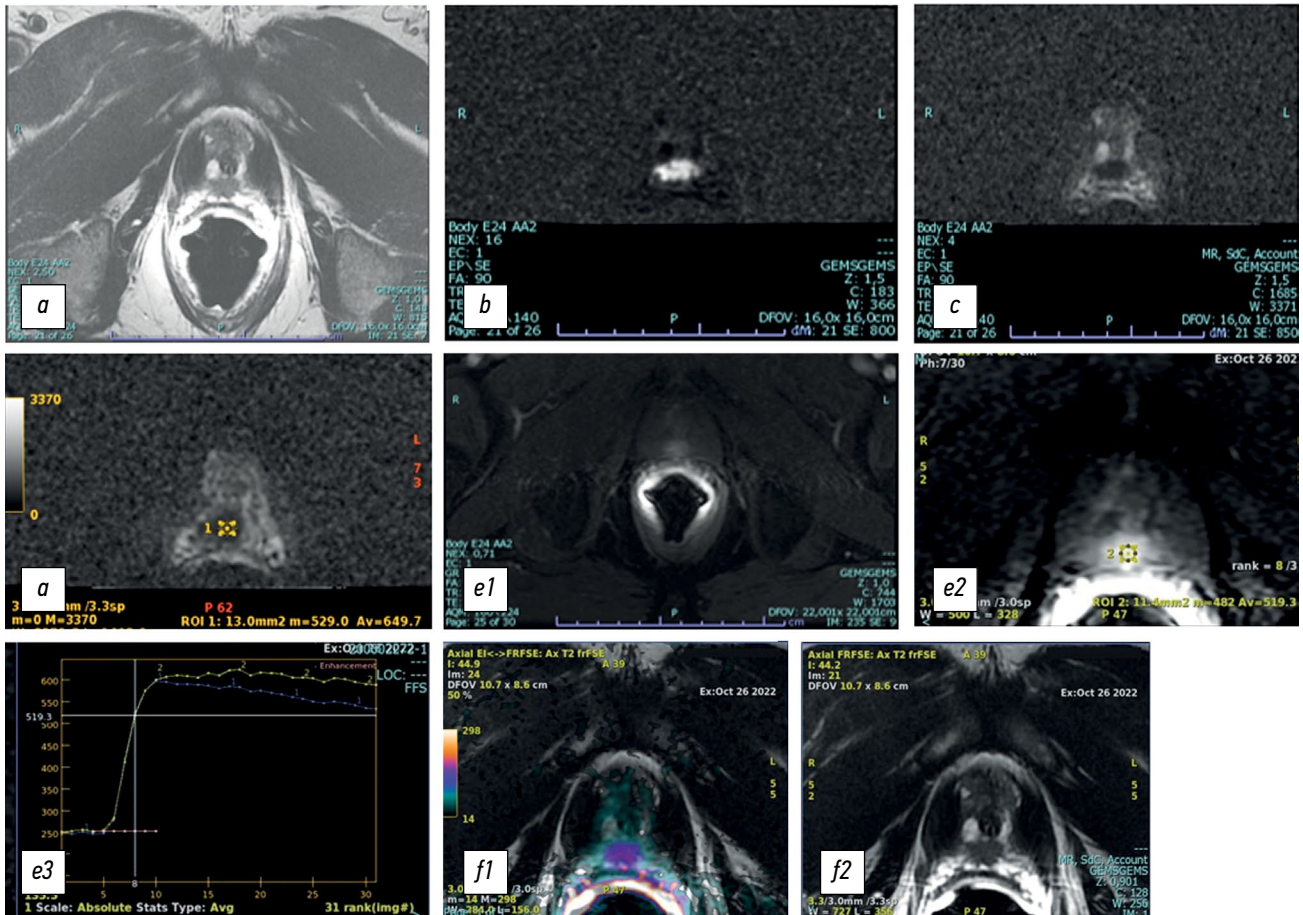


Fig. 1. T2-weighted (a) magnetic resonance image (axial plane) showing a hypointense nodular lesion in the peripheral zone at the apical posterior site. Axial diffusion-weighted MR image (b) with an apparent diffusion coefficient (ADC) (c) of put value $\times 10^{-3} \text{ m}^2/\text{sec}$ in the corresponding area. Reduced water diffusion in prostate cancer (PCa) is related to increased cellularity of malignant lesions, with a reduction in the extracellular space and restriction of movement of a larger portion of water molecules into the intracellular space. Therefore, DWI with the corresponding ADC map provides an important quantitative biophysical parameter that can be used to diagnose PCa (d). The tumor is characterized by intense early hyperenhancement of the normal adjacent tissue (e). Colorimetric map generated by the DCE evaluation of PCa in the peripheral area at the apical site. The suspicious area is coded in red (f).

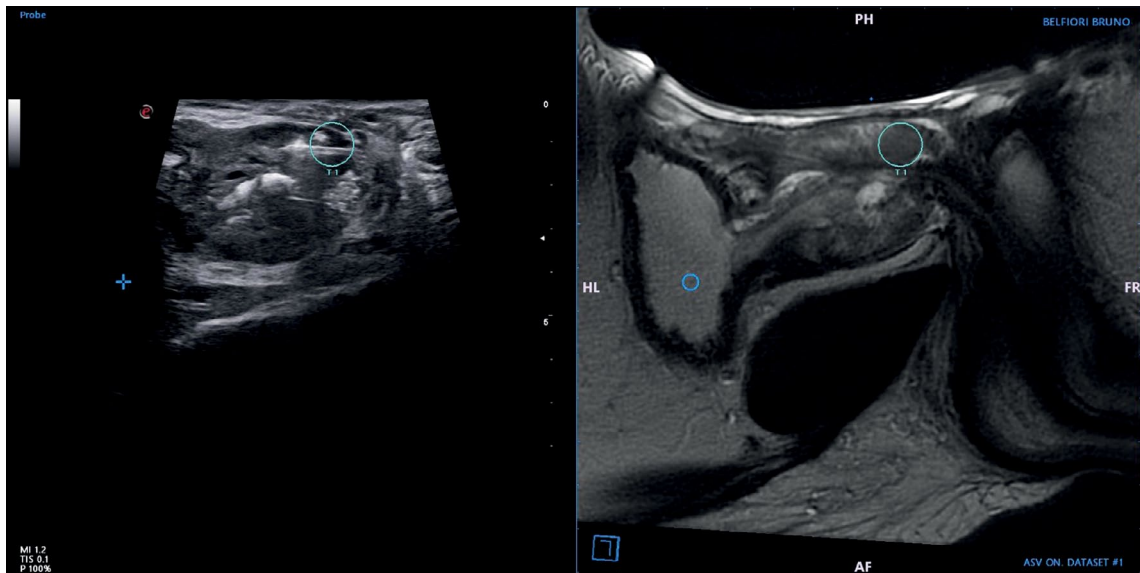


Fig. 2. MRI-TRUS fusion-guided prostate biopsy. The prostate and lesions identified on MR images (in this case, on T2W imaging) are segmented. During the procedure, a 2D TRUS scan of the prostate was performed. Images were recorded semiautomatically. Co-viewing images can be tiled or overlaid. By merging the two images, the urologist can locate the lesion during a biopsy using real-time ultrasound guidance.

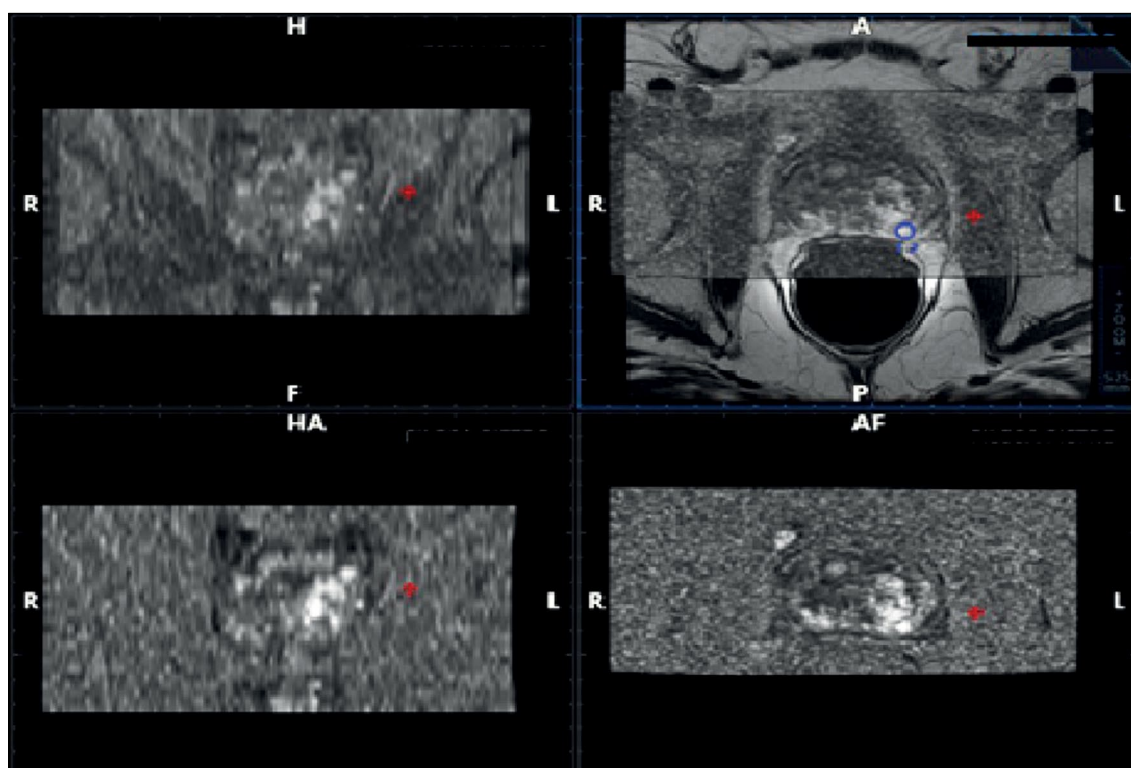


Fig. 3. Magnetic resonance (MR) imaging of prostate cancer: axial diffusion-weighted MR image (up on the left) with an apparent diffusion coefficient map (down on the left), T2-weighted MRI image (up on the right), and T1-weighted image after contrast media (down on the right).

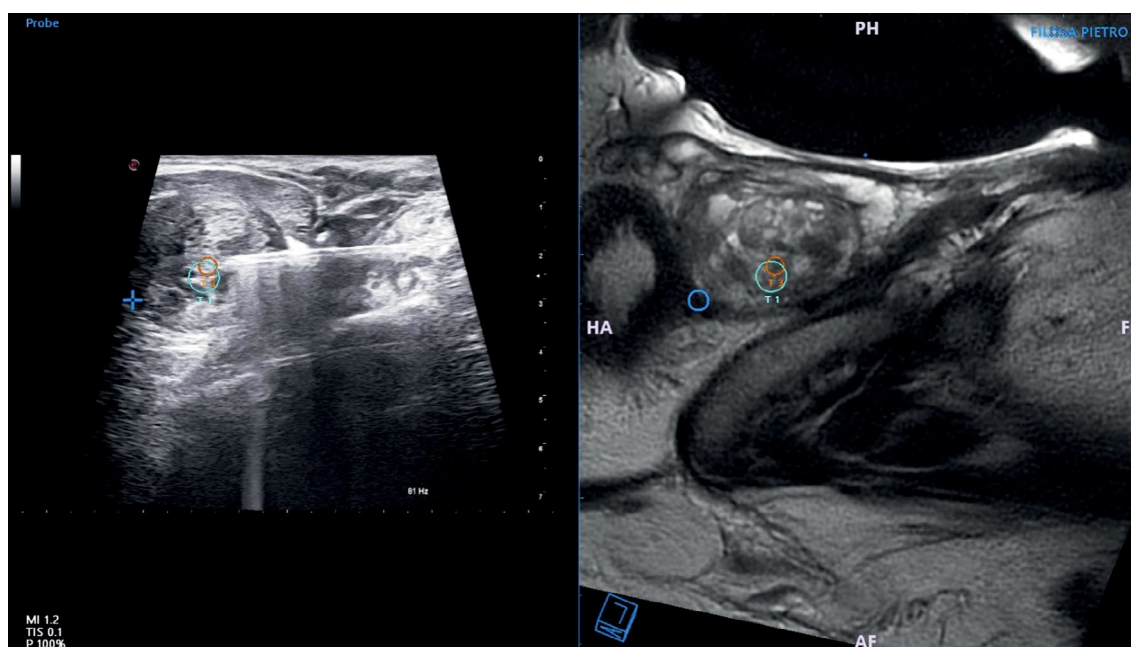


Fig. 4. Magnetic resonance imaging is fused with real-time TRUS using a digital overlay, allowing the target(s) previously delineated by a radiologist to be brought into the ultrasound machine's aiming mechanism. Fusion enables the reconstruction of the prostate, and the aiming and tracking of biopsy sites occur on the reconstructed model.

also employ dynamic repeat registration methods using motion-compensation algorithms to guarantee accurate and reproducible index lesion targeting [12].

Recent studies have compared the detection of PCa and severe disease using traditional SB or TPMB as a reference test [22, 28, 29].

In a cohort of >1000 patients, Siddiqui et al. used the Uronav system and conventional 12-core TRUS-guided biopsy as a reference test and reported that TB diagnosed 30% more high-risk cancers than standard biopsy ($P = 0.001$) and 17% fewer low-risk cancers ($P = 0.002$) using primary GS 4 as the significance level [22]. Rastinehad et al. defined GS 3 + 4 as

clinically significant PCa (sPCa) and reported that 14.3%–20.9% of sPCa cases were discovered by TB alone but ignored by the traditional TRUS technique [30]. Furthermore, 23.5% of cases were upgraded from insignificant to sPCa through MRI–TRUS fusion-guided biopsy [30]. In contrast, 4/105 sPCa cases were missed by MRI–TRUS fusion-guided biopsy [30].

Baco et al. demonstrated that 98% of index tumors defined as the highest GS or biggest volume in the case of multifocality with equal GS, were diagnosed by MRI and that 98% of the correct location was diagnosed by MRI–TRUS fusion-guided TB using the Koelis Urostation® [31].

Regarding public health, Cerantola et al. published a cost-effectiveness analysis comparing TRUS biopsy with MRI target biopsy (MRTB) in 2016. They assessed the cumulative effects after 5, 10, 15, and 20 years and determined that including MRI and MRTB in PCa diagnosis and care is a cost-effective measure after 5, 10, 15, and 20 years [32].

COMPARATIVE STUDIES OF DIFFERENT TARGETED BIOPSY APPROACHES

Only a few studies have examined the CDRs of various targeting strategies, and the results are contradictory [26].

Delongchamps et al. reported that cognitive fusion biopsy was not significantly better than SB in a study comparing VE with two MRI–TRUS fusion devices; however, both software coregistration devices tested (Esaote/MyLabTMTwice and Koelis/Urostation) significantly increased the CDRs compared with SB in a cohort of 391 patients using conditional logistic regression analysis [33].

In a prospective trial of 125 men with worrisome lesions, Wysock et al. compared MRI–TRUS fusion-guided biopsies using the Eigen/Artemis system with VE targeting [34]. They found that MRI–TRUS fusion-guided biopsies had a slightly improved CDR compared with VE for all cancers (32% vs. 26.7%, $P = 0.1374$) and for GS $\geq 3 + 4$ (20.3% vs. 15.1%, $P = 0.0523$).

Puech et al. found no difference in the CDR of PCa for rigid software coregistration using MedCom Navigator versus cognitive fusion TB (53% vs. 47%). Furthermore, no variations in cancer positivity were observed in the categories of posterior (46 of 79, 58%), anterior (33 of 79, 42%), or smallest (25 of 79, 32%) MRI targets [15]. In 2013, Bjurlin et al. conducted a literature review, and their findings indicated that the use of MRI to target prostate biopsies can reduce sampling errors associated with conventional biopsy by providing better disease localization and sampling. They discovered that increased cancer sampling allows more accurate risk classification, which may influence therapeutic decision making. However, the best clinical application of MRB has not yet been determined [3].

EARLY DETECTION OF PROSTATE CANCER

The US Preventive Services Task Force (USPSTF) updated its recommendations in 2018, largely based on the publication

of longer follow-up data from large screening trials and emerging evidence that the use of AS in low-risk PCa reduces the harms associated with screening overtreatment. The USPSTF now recommends that men aged 55–69 years undergo PSA testing following a discussion with their clinicians about the relative benefits and harms, although it still advises against PSA screening in younger men (aged 40–55 years) or those aged >70 years [35].

In the absence of widespread organized PSA testing, opportunistic testing has become a routine practice in many EU member countries. However, a recent study revealed that while this strategy has minimal influence on PCa-specific mortality, it is associated with overdiagnosis than organized risk-adapted PSA testing [36]. This lack of effect is largely attributed to testing individuals who will not benefit (e.g., those with a 10-year life expectancy) without sufficient informed decision making [37], as well as repeated testing in men who are not at risk of developing severe PCa [38].

Overdiagnosis can be reduced by employing a risk-adapted detection strategy based on PSA values in conjunction with risk calculators and mpMRI, which can distinguish between significant and insignificant PCa and modify treatment accordingly. As a result, many cases of early PCa diagnosis can be handled with AS, thereby avoiding overtreatment [39]. Those with a lower-risk profile may benefit from local treatment, which has fewer adverse effects and produces better results than if the condition was diagnosed and treated later, thereby enhancing or maintaining the patient's quality of life [40].

The EAU has created an algorithm to explain a risk-adapted strategy for PCa detection. This algorithm is intended for use in well-informed men aged >50 years with a life expectancy longer than 10–15 years. This algorithm clearly demonstrates how to achieve early detection of serious PCa while avoiding overdiagnosis and overtreatment. Following a clinical risk assessment and appropriate counseling, the PSA test represents the first step in identifying a large proportion of men with a low PSA value who do not require any further immediate investigations for 2–4 years (for those with a PSA value of 1–3 ng/mL) or 5 years (for those with a PSA value of 1 ng/mL and aged 60 years) [39].

A risk stratification nomogram (which considers factors such as age, family history, digital rectal examination, and prostate volume [PSA density] in a risk calculator) will identify a subgroup of men (approximately 35% of all men with an initial PSA test of >3 ng/mL [41]) as those with a low risk who require clinical follow-up only, avoiding the need for further testing, including MRI and biopsy. Men with a PSA value of >3 ng/mL who were classified as intermediate or high risk would then undergo mpMRI, leading to the identification of a further subgroup (approximately 54% of all men undergoing MRI [41]) with a Prostate Imaging Reporting and Data System (PIRADS) score of 1–2 considered at a low risk of having sPCa and requiring clinical follow-up only.

Further risk categorization of men with a PIRADS score of 3 using PSA density and other clinical characteristics would reveal an additional category requiring only clinical follow-up (a PIRADS score of 1, 2 or “low-risk” 3 accounts for approximately 57% of men tested by PIRADS [41]). As a result, the remaining subset of the original population could be regarded as intermediate or high risk and should undergo targeted and/or systematic biopsy. Within this subgroup, those with a positive diagnosis and a favorable grading group (approximately 25% of all confirmed diagnoses [41]) may be eligible for AS rather than active treatment.

However, as part of a collaborative decision-making process, all final treatment decisions should consider the patient’s values and preferences [40]. This algorithm demonstrates how PSA testing can be used more intelligently by incorporating risk calculators, such as those developed by the European Randomised Study of Screening for PC (ERSPC) and the Prostate Cancer Prevention Trial [42], as well as mpMRI and the Pirads score [43, 44], to reduce the number of men undergoing biopsy. The proposed time intervals for repeat PSA testing depending on age and initial PSA test result reflect the risk of a future clinically significant cancer diagnosis [45] and thus help reduce false-positive biopsies.

The risk calculator to be used must also be carefully selected. Although the ERSPC risk calculator has been well verified and may thus be regarded as superior, a recalibration step may be required to account for regional variations in prevalence and the link between PSA and PCa risk [46].

CANCER RISK ASSESSMENT USING TARGET BIOPSY

The change from systematic biopsy to image TB raises significant concerns regarding the clinical care of PCa. More men should choose AS if new biopsy techniques provide them with greater confidence.

However, the use of targeted biopsies will be exploited to justify additional overtreatment. Currently, risk classification systems based on biopsy results greatly affect therapy decisions [47]. These systems evolved from traditional systematic biopsies. When tumors are sampled more thoroughly with TB, the proportion of positive cores and maximum CCL are higher than with traditional biopsy [48,18].

As a result, compared with systematic biopsy, TB increased risk attribution. In a computer simulation study that included 107 reconstructed 3D models of whole-mount prostatectomy specimens, Robertson et al. [49] revealed this critical issue. They discovered that a 12-core TRUS biopsy properly categorized only 24% of clinically significant cancer-containing prostates as high risk, compared with 74% of cases using a transperineal TB with four cores. Furthermore, the targeted biopsies had a higher proportion of positive cores and higher maximum CCLs. They concluded that when risk models derived from conventional TRUS biopsy

are used for image-directed biopsy, there is a systematic rise in risk attribution.

At UCLA, one hundred and ninety-four AS men were treated with MR-US fusion TB, which included systematic and targeted sampling. Using only systematic biopsy and the Epstein histological criteria (Gleason score 6, 2 cores cancer, and 50% of any core), 28% of men were categorized as poor candidates for surveillance on confirmatory biopsy.

Incorporating TB increased the number of reclassified patients to 41%. In some circumstances, this is caused by the discovery of additional dangerous malignancies, whereas in others (i.e., numerous malignant cores from a single MRI target), it is the result of using a classification system that does not consider TB.

Given the inflation in risk attribution, TB may be used to justify aggressive treatment of more men, exacerbating the overtreatment problem. To avoid this unwanted effect, new risk stratification criteria based on image-targeted biopsy must be developed and verified. Consider a man who underwent a conventional biopsy with a low-volume GS of 3 + 3 and a TB with a low-volume GS of 3 + 4. TB combined with device-based tracking of malignant detects could be used to safely follow tumors that are now thought to require treatment [47].

INCORPORATION OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING FUSION-GUIDED BIOPSY WITH RISK MODELING FOR PROSTATE CANCER

When compared with RP specimens, mpMRI detects 85%–95% of index lesions and sPCa [50]. The use of TB of dubious mpMRI lesions in a fusion biopsy context increases the identification of sPCa by 30% [22].

Multivariate risk-based techniques have been established to identify men with sPCa while avoiding needless biopsies [51,52]. A risk calculator based on data from the ERSPC was created to quantify the sPCa risk. Roobol et al. revealed that in men with a PCa risk of 12.5%, 33% of routine biopsies might be avoided [52].

Although TB of mpMRI-suspicious lesions alone is a potential technique for reducing the overdetected of minor illnesses, MRI-invisible sPCa can be missed [22, 53, 54].

Unlike Alberts et al., Radtke et al. and van Leeuwen et al. developed risk calculators and added prebiopsy mpMRI to clinical parameters to determine an individual sPCa risk using a validated biopsy approach combining fusion-guided TB and transperineal systematic SBs as reference on the one hand and transperineal mapping and TB plus 12-core TRUS on the other [55, 56].

In the area under the curve (AUC) of the receiver operating characteristics curve analysis, Van Leeuwen et al. demonstrated that a model combining age, PSA, DRE, prostate volume, previous biopsy result, and mpMRI Pirads Likert score outperformed the model of clinical parameters

alone with discrimination of 0.90 [56]. In addition to the model for biopsy-naïve men, Radtke et al. internally validated a risk model for men with a previous negative biopsy that combined PSA, prostate volume, DRE, age, and mpMRI Pirads Likert scoring [55]. When compared with a validated clinical parameter risk calculator and Pirads, the model beat both instruments [55]. When risk models that include mpMRI and clinical parameters are compared with risk models that only use clinical parameters or PIRADS, the accuracy of the decision to perform a biopsy in a patient with sPCa suspicion can be increased. In conclusion, risk models that include mpMRI are superior to risk models that exclude mpMRI not only for men before initial biopsy but also for patients who have had previous negative biopsy results [55, 56].

While detection of sPCa can be improved, an unsuspecting mpMRI or a low PIRADS score cannot be used to justify not proceeding with a biopsy in the case of PCa suspicion. MRI fusion biopsy was claimed to help diagnose indolent PCa. However, finding low-risk PCa can improve patient safety by avoiding unnecessary treatment and improving disease monitoring accuracy and reliability when selecting individuals for AS.

Avoiding Multiparametric Magnetic Resonance Imaging Fusion Biopsy Failure

Although mpMRI offers helpful details regarding the diagnostic route for sPCa, mpMRI fusion biopsy can fail. To date, four potential mechanisms for mpMRI fusion biopsy failure have been identified: mpMRI-invisible cancer, improper sampling, mpMRI reader oversight, and intralesion GS heterogeneity [57]. Muthigi et al. demonstrated that in 71% of cases when SB discovered sPCa but TB did not, the malignant finding was within the sextant of the target lesion, correlating with the findings of Cash et al., who identified inaccurate sampling as one of the primary causes of fusion biopsy failure [58].

Similarly, Bryk et al. identified a combination of TB and ipsilateral SB as the best strategy to detect sPCa and avoid detection of low-risk PCa in patients with unilateral mpMRI lesions using TB, and both sided SB as a reference [59]. The findings of these two studies imply that increasing the number of samples taken from the target area can help minimize erroneous sampling and intralesion GS heterogeneity. However, Porpiglia et al. discovered that two targeted cores inserted in the center of the lesion are sufficient to precisely portray the index lesion [60].

More research on this topic is required. The mpMRI fusion biopsy failure caused by mpMRI-invisible cancer, which has a consistent negative predictive value (NPV) for mpMRI of 63%–98%, can only be solved with further SB [61, 62]. However, most groups that combined TB with 12-core SB found no substantial benefit in detecting sPCa by combining both approaches over TB alone [22, 63].

In contrast, Filson et al. discovered that the combination biopsy approach detected much more sPCa than TB or SB alone [64].

These controversial results lead to the conclusion that the superiority of sPCa detection in a combined biopsy approach compared to a TB-only approach increases with the amount of SB, but with the risk of finding significantly lower-risk diseases.

The question of whether to omit SB might never be entirely solved, and decisions should be made individually according to biopsy indications and patient needs.

The technique used to perform the biopsy is another point regarding the quality and possible reasons for failure of mpMRI fusion biopsy.

MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING FUSION-GUIDED BIOPSY IN MEN REQUIRING A REPEAT BIOPSY

Men with a previous negative biopsy and an ongoing suspicion of PCa should be continuously monitored. Prior sampling reduces overall disease incidence relative to a biopsy-naïve group; however, individuals with continuous suspicion for PCa suffer from inadequate NPV of 12-core TRUS-guided biopsy. MpMRI has been proven in many studies to be effective in monitoring this patient group and should thus be suggested in a repeat biopsy setting [65, 1].

Most recent studies have examined these patients as a subset of a larger cohort; however, some studies have paid special attention to this patient group: Simmons et al. evaluated the diagnostic accuracy of mpMRI in men requiring repeat prostate biopsy (PICTURE study), although only 31% of men had a previous negative biopsy [66]. When used as a positive test result, an mpMRI score of 3 has a sensitivity of 97%, specificity of 22%, NPV of 91%, and positive predictive value of 47% [66].

The authors conclude that a repeat biopsy can be avoided in 14% of men at the cost of missing 9% of sPCa [66]. Hansen et al. reported a significantly improved AUC when Pirads and PSA density were combined (0.82 vs. 0.85), implying that repeat biopsy should be avoided only in cases of worrying mpMRI and low PSA density [67]. Again, data are unclear on when it is safe to exclude SB. Arsov et al. compared in-bore TB to fusion-guided TB plus 12-core TRUS-SB in a prospective randomized experiment. They discovered that adding SB had no further benefit in detecting sPCa [10].

In contrast, recent papers comparing TB alone methods with 24- or 12-core SB reveal that TB alone misses a significant amount of sPCa [67].

MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING FUSION-GUIDED BIOPSY IN MEN UNDER AS

Men with PCa who are eligible for AS are another important patient category because proper risk assessment of potentially less serious conditions is essential. To achieve this purpose, mpMRI in conjunction

with fusion biopsy can aid in initial candidate screening and disease progression monitoring. Radtke et al. analyzed in a sample of 149 men whose initial mpMRI and fusion biopsy before AS resulted in significantly reduced rates of later AS qualifying (20% vs. 48%) during a 2-year follow-up compared with those selected for AS based on 12-core TRUS-guided biopsy [68].

These findings are supported by Henderson et al., who revealed in a prospective study that the apparent diffusion coefficient (ADC) is a good marker for choosing patients for AS because a low ADC value is associated with a shorter time to unfavorable histology [69]. Several recent studies have examined mpMRI and fusion biopsy for disease progression detection. Most of them reveal that mpMRI accurately predicts the likelihood of clinical progression and that patients with stable mpMRI findings have a low probability of developing the disease [70–72].

The inclusion of clinical criteria in the decision-making process appears to be advantageous when selecting patients for AS. Alberts et al. discovered in a cohort of 210 men without upgrade at baseline, confirmatory, or surveillance biopsy in instances of unsuspicious mpMRI and PSA density <0.15 ng/mL, implying that follow-up biopsy should be avoided in these individuals [10]. However, whether following up with fusion biopsy confined to mpMRI-visible targets is sufficient is still being debated. Meng et al. and Frey et al. showed that on combined SB and TB follow-up mpMRI fusion biopsy, TB detected significantly more upgrades than SB, supporting the rationale for removing SB [70, 53].

Conversely, Tran et al., Ma et al., and Recabal et al. found that a significant fraction of higher-grade malignancies could only be diagnosed by SB, suggesting the necessity for additional SB [71, 72]. These contradictory results can be explained in part by differences in study parameters such as median TB and SB cores; however, they also highlight the need for additional research on long-term results, serial mpMRI for replacing repeat biopsies, and sufficiency of follow-up biopsies limited to mpMRI targets.

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CONCLUSIONS

MRTB improves the quality of histological results compared with other approaches, with a correct detection of approximately 90% of significant index lesions.

The systematic 12-core TRUS-guided biopsy is still a widely used technique despite its limited sensitivity for the clinical detection of sPCa.

MRI-guided biopsies provide a higher detection rate for clinically detected sPCa and increase the percentage of positive cores.

Although currently used in patients who remain at high clinical suspicion of PCa despite a negative TRUS-guided systematic biopsy, with the increasing use of upfront diagnostic MRI, these biopsies are expected to replace standard systematic biopsies.

Correct staging allows the selection of the best treatment options, including focal treatments, and adequate evaluation of the prognosis. It also reduces the incidence of re-biopsy, costs, and complications.

It is crucial to standardize the bioptic technique and improve the fusion technique to reduce understaging caused by errors in estimating the tumor volume. The role of mpMRI in the presurgical phase of RP is emerging because mpMRI can help in planning the initial surgical strategy, referring to clinical decision making.

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AUTHORS' INFO

* **Giuseppe Guglielmi**, MD, Professor;
ORCID: 0000-0002-4325-8330;
e-mail: giuseppe.guglielmi@unifg.it

05 ABTOPAX

* **Giuseppe Guglielmi**, MD, Professor;
ORCID: 0000-0002-4325-8330;
e-mail: giuseppe.guglielmi@unifg.it

* Corresponding author / Автор, ответственный за переписку

Valentina Testini, MD;
ORCID: 0000-0003-1231-5213;
e-mail: testinivalentina@gmail.com

Laura Eusebi, MD;
ORCID: 0000-0002-4172-5126;
e-mail: lauraeu@virgilio.it

Francesco Saverio Guerra, MD;
ORCID: 0000-0003-3923-3429;
e-mail: francesco.rino@gmail.com

Willy Giannubilo, MD;
e-mail: willygiannubilo@virgilio.it

Manuel Di Biase, MD;
e-mail: manuel.dibiase@ospedale.perugia.it

Annunziata Russo, MD;
ORCID: 0000-0002-4643-4280;
e-mail: tittyrusso-23@libero.it

Valentina Testini, MD;
ORCID: 0000-0003-1231-5213;
e-mail: testinivalentina@gmail.com

Laura Eusebi, MD;
ORCID: 0000-0002-4172-5126;
e-mail: lauraeu@virgilio.it

Francesco Saverio Guerra, MD;
ORCID: 0000-0003-3923-3429;
e-mail: francesco.rino@gmail.com

Willy Giannubilo, MD;
e-mail: willygiannubilo@virgilio.it

Manuel Di Biase, MD;
e-mail: manuel.dibiase@ospedale.perugia.it

Annunziata Russo, MD;
ORCID: 0000-0002-4643-4280;
e-mail: tittyrusso-23@libero.it