Résumé
Écho-Doppler et cancer de la prostate : option ou nécessité ?
J Radiol 2006;87:1063-72

Objectifs. Déterminer la valeur de l’Écho Doppler Puissance (EDP) dans le diagnostic et le bilan d’extension des cancers prostataques.

Matériels et méthodes. 579 patients présentant un taux sérique de PSA supérieur à 3,5 ng/ml ont fait l’objet d’un examen EDP avant chaque série de biopsies. 6 biopsies initiales ont été réalisées en sextant sans Doppler. 141 patients gardant une sérologie de PSA anormale ont subi une série complémentaire de 6 à 8 biopsies sous guidage EDP.

Résultats. Une anomalie caractérisée par une zone hypoechogène et/ou hypervasculaire (hypertrophie de vaisseaux normaux ou anormaux) était présente à l’EDP chez 335 patients et correspondait dans 260 cas à un cancer. Trente neuf cancers ne présentaient aucune anomalie à l’examen écho Doppler. La valeur prédictive négative (VPN) de l’EDP était évaluée globalement à 84 % : les VPN calculées pour chaque sous-groupe de patients classés en fonction de leur taux de PSA ne montraient pas de différence statistiquement significative entre elles (p < 0,01). Après la première série de biopsies négatives si une anomalie persistait à l’EDP, le risque d’avoir une biopsie positive sur la série complémentaire échoguidée était de 83 %. La présence de vaisseaux anormaux hypertrophiés était corrélée au degré de différenciation cellulaire de la lésion (p < 0,001) : 69 % des patients avec un score de Gleason > ou égal à 7 présentaient des vaisseaux anormaux contre seulement 31 % des patients avec un score de Gleason < a 7. Parmi les 39 cancers non visibles à l’EDP et non palpables, 35 avaient un score de Gleason < ou égal à 6. Vingt ont fait l’objet d’une PR : dans 11 cas les lésions étaient considérées comme insignifiantes. Après prostatectomie radicale le caractère le plus pertinent pour diagnostiquer une extension extraprostatique (EEP) avec l’EDP était la recherche de vaisseaux d’origine tumoraire franchissant la capsule : une EEP était alors présente dans 71 % des cas (sensibilité : 37,5 %, Spécificité : 91 %, VPN : 78 %) (p < 0,01).

Conclusions. L’EDP peut contribuer à l’évaluation du degré d’agressivité de chaque cancer prostatique et limiter le nombre des biopsies utiles au diagnostic.


Abstract
Power Doppler Imaging and prostate cancer: optional or necessary technique?

Purpose. To evaluate the value of power Doppler sonography (PDS) in patients with a serum PSA level greater than 3.5ng/ml and note the advantages of PDS in management of biopsy cores and staging in prostate cancer.

Material and methods. A group of 579 patients with a serum PSA level greater than 3.5ng/ml underwent sextant biopsies. PDS of the prostate was performed in all patients before biopsy indication. Patients underwent six initial sextant biopsies without Doppler. In 141 patients who retained an elevated serum PSA level, an additional series of six to eight ultrasound-guided biopsies with Doppler were indicated. A total of 299 cancers were diagnosed (126 palpable) after initial biopsies and 85 (13 palpable) after additional biopsies. One hundred seven patients with localized cancer (48 palpable) underwent a radical prostatectomy.

Results. An echographic or vascular anomaly was detected in 335 patients; after biopsies this anomaly corresponded to 260 cancers, 39 of which were not visible (false-negative Doppler results). The negative predictive value was 84% and there was no significant relation between PSA level and negative predictive value. After initial biopsies, if an abnormal Doppler signal was present the risk of having positive additional biopsies was 83%. Abnormal disoriented irregular vessels were present in 69% of patients with a Gleason score of 7 or higher versus 31% in patients with a Gleason score less than 7 (p<0.01). Twenty out of 39 patients with T1c cancer invisible with PDS and not palpable (13% of all cancers) underwent a radical prostatectomy. Eleven of 16 cancers with a Gleason score of 6 or less were found insignificant, but in two cases the lesion was advanced (p<0.01). Of cancers with a tumor vessel crossing the capsule, 71% presented an extraprostatic extension (Se: 37.5%, Spec: 93%, PPV: 71%, NPV: 78%) (p<0.01).

Conclusion. In prostate cancer, PDS allows evaluation of aggressiveness features and can optimize the number of useful biopsy cores.

Key words: Prostate. cancer. ultrasonography. Doppler and power Doppler imaging.

prostate cancer, a thorny problem in oncology today, is frequent and long remains silent. Screening with a serum marker, PSA, has provided a constant increase in the incidence of prostate cancer diagnosed in France (1). Some authors claim that this screening is positive because the earlier the diagnosis is made the greater is the hope for cure (2). For others, this screening may be the cause of overdiagnosis (3-6).

Histological diagnosis is currently established based on a protocol of 12 initial biopsies that can be expanded up to 45 biopsies in certain saturation protocols necessary for initial diagnosis; 85 with 7-10 biopsies based on precise and systematic sector mapping (7-10).

Staging is based on comparing the results of the serum PSA levels (11), the degree of the tumor’s tissue differentiation, the number of positive biopsies, and for some the length in millimeters of the tumors on these biopsies (quantitative histology). Statistical tables or nomograms integrate these different factors to predict the statistical risk of metastases (12) or recurrence depending on the choice of therapy.

Prostate cancer diagnosis and staging do not depend on imaging, which remains an optionnal technique that is usually not recommended. Endoluminal ultrasonography combined with color or power Doppler examination before the radical prostatectomy is part of this prostatic imaging: it has been the subject of many, often contradictory, publications. Since all cancers are not hypoechogenic or hypervasculaire, ultrasound and Doppler give many false-negative results (13); however, 2D sonography can often localize the main tumor focus in relation to the base or apex, color Doppler can evaluate the degree of tumor vascularization (14-19), guide and limit the number of biopsies (20-22), and some authors claim that color Doppler (14) and 3D Doppler (23) can predict extracapsular extension. The question of whether false-negative results are related to less aggressive lesions can also be raised (24), which could lead to less restrictive management strategies.

The goal of this study was to determine, from a series of patients presenting a serum PSA level greater than 3.5 ng/ml:

- the negative predictive value and the significance of power Doppler sonography (PDS);
- the role of power Doppler in the biopsy protocols necessary for initial diagnosis;
- The possible value of PDS in the search for signs of tumor aggression in the staging of diagnosed cancers.

### Materials and methods

#### Patients

Five hundred seventy-nine patients (49-87 years, mean age, 68 years; median age, 71 years), seen between January 1999 and October 2004, presenting a serum PSA level over 3.5 ng/ml had sextant biopsies (mean PSA, 18.2 ng/ml; median, 10 ng/ml, from 3.5 to 500 ng/ml) (table I). Two hundred ninety-nine cancers where diagnosed, 214 with 126 palpable lesions after the initial series of biopsies and 85 with 13 palpable lesions after a second series of additional biopsies.

One hundred seven patients (mean age, 65 years; median age, 67 years) with clinically localized cancer underwent a radical prostatectomy (mean PSA, 10 ng/ml; median PSA, 11.9 ng/ml): they were included in a prospective study that investigated extraprostatic extension and had a power Doppler examination before the radical prostatectomy. Of these 107 cases of cancer undergoing surgery, 48 tumors were palpable (table II).

#### Table I

<table>
<thead>
<tr>
<th>PSA(ng/ml)</th>
<th>PSA ≤ 10</th>
<th>PSA &gt; 10</th>
<th>P</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP</td>
<td>100</td>
<td>160</td>
<td></td>
<td>260</td>
</tr>
<tr>
<td>TN</td>
<td>132</td>
<td>73</td>
<td></td>
<td>205</td>
</tr>
<tr>
<td>FP</td>
<td>48</td>
<td>27</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>FN</td>
<td>25</td>
<td>14</td>
<td></td>
<td>39</td>
</tr>
<tr>
<td>TOTAL</td>
<td>305</td>
<td>227</td>
<td></td>
<td>579</td>
</tr>
<tr>
<td>Se</td>
<td>80</td>
<td>92</td>
<td>&lt; 0.01</td>
<td>87</td>
</tr>
<tr>
<td>Spe</td>
<td>73</td>
<td>73</td>
<td>NS</td>
<td>73</td>
</tr>
<tr>
<td>PPV</td>
<td>68</td>
<td>86</td>
<td>&lt; 0.01</td>
<td>78</td>
</tr>
<tr>
<td>NPV</td>
<td>84</td>
<td>84</td>
<td>NS</td>
<td>84</td>
</tr>
</tbody>
</table>

Results of power Doppler sonography in 579 patients after two series of prostatic biopsies depending on PSA level (VP: true positive, FP: false positive, VN: true negative, FN: false negative, Se: sensitivity, Spe: specificity, VPP: positive predictive value, VPN: negative predictive value, NS: not significant).

#### Table II

Prospective study after radical prostatectomy in 107 patients: comparison of histological results in true-positive and false-negative patients after power Doppler sonography.

<table>
<thead>
<tr>
<th>PSA (ng/ml)</th>
<th>PSA ≤ 10</th>
<th>PSA &gt; 10</th>
<th>P</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>4-28</td>
<td>4-27</td>
<td>4-27</td>
<td>4-26</td>
</tr>
<tr>
<td>Mean</td>
<td>11.46</td>
<td>12.02</td>
<td>11.21</td>
<td>12.88</td>
</tr>
<tr>
<td>Median</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Number of anterior/ peripheral lesions</td>
<td>2/18</td>
<td>9/79</td>
<td>5/53</td>
<td>4/26</td>
</tr>
<tr>
<td>Mean Gleason score grade 4 or 5</td>
<td>5.3</td>
<td>6.29</td>
<td>6.14</td>
<td>6.88</td>
</tr>
<tr>
<td>Median</td>
<td>5/20</td>
<td>43/87</td>
<td>23/67</td>
<td>36/75</td>
</tr>
<tr>
<td>T2a+b</td>
<td>15</td>
<td>5</td>
<td>48</td>
<td>36</td>
</tr>
<tr>
<td>T2c</td>
<td>39</td>
<td>21</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>TNM clinical stage</td>
<td>insignificant</td>
<td>15</td>
<td>5</td>
<td>48</td>
</tr>
<tr>
<td>pT2a</td>
<td>4</td>
<td>23</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>pT2b or pT2c</td>
<td>3</td>
<td>34</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>pT3a or pT3b</td>
<td>1</td>
<td>24</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>pT3c</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>

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The therapeutic decision was taken on the basis of criteria defined and recommended by the French Association of Urology, including patient age, clinical stage, PSA level, and Gleason score. A 5-year nonrecurrence risk factor after surgical treatment was evaluated by the nomogram described by Kattan et al. (12).

Biopsies and examination of radical prostatectomy specimens

Each patient included in our series underwent a power Doppler examination before the biopsies. The urology department did not have ultrasonography equipped with 3D Doppler; consequently the initial biopsies (a single biopsy per sextant) were done by a surgeon, without taking into account the results of the Doppler examination, according to Hodge’s protocol (25). In 141 patients (mean PSA, 11.4ng/ml; median PSA, 8ng/ml) retaining an abnormal serum PSA level 6 months after the initial biopsies, a second series of power Doppler-guided biopsies, which completed the first series by adding more lateral samples, was carried out: seven to eight samples were taken, one per sextant in the subcapsular zone and one to two samples in the suspicious zones as shown on the Doppler examination and/or on ultrasound. When the prostate was normal on the Doppler examination and with ultrasound, two additional biopsies in the transition zone were added.

Examination of the radical prostatectomy specimen provided the pT classification. Capsular penetration was focal if only a few cells were present outside the capsule or established if there was more substantial invasion (26). The Gleason score was determined for each tumor. Eight patients presenting an isolated positive margin with no periprostatic tissue and no sign of capsular penetration were classified as pT2 with a positive margin. A tumor with a Gleason score less than or equal to 6 and staged as T1c was considered potentially insignificant after biopsies if a single core biopsy was positive with a tumor length less than 3 mm (27).

Sonography semiology and power Doppler

B mode localized a possible intraprostatic lesion among the different sextants and detailed its size, its echostructure (hypoechoic, slightly hypoechoic or subtle, hyperechoic, heterogenic). The power Doppler (2D and 3D) searched for the presence of normal intraprostatic blood vessels (regular, nondisoriented vessels, in a normal situation that could be hypertrophied) (fig. 1) or abnormal blood vessels (irregular, sinuous, or disoriented vessels) (fig. 1) (21, 29). A visible lesion in B mode was labeled hypervascularized if it included one or several vessels. If it was less than 5 mm in size the lesion was qualified as focal (fig. 3). If the lesion measured more than 5 mm, but was confined to a single sextant, and included vessels of the vascular bed that were strictly intrasessional, this lesion was qualified as nodular (fig. 1). If the hypoechoic zone concerned three sextants or more, and/or the vessels extended beyond the hypoechoic zone, the lesion was qualified as infiltrating (fig. 4). In cases of a nodular lesion associated with other foci with no real contiguity, the lesion was qualified as multifocal. An isolated vascular asymmetry with no associated hypoechoic lesion suggested an isoechogenic lesion (fig. 5). A lesion was said to be subtle if it was confirmed only by vascular asymmetry on the Doppler because of its low hypoechoegenicity (fig. 6). When an intrasessional blood vessel perforating the capsule was observed, an extraprostatic extension was suspected (fig. 7).

Statistical analysis

The results of the imaging study were correlated with the pathological examinations. A result was declared true positive if at least one biopsy was positive in the same sextant as the lesion visualized. A result was declared true-negative if no biopsy was found positive during the examination with no lesion visible. Sensitivity, specificity, and positive and negative predictive values of cancer diagnosis were calculated; significance was evaluated using the chi square test \( (p<0.05) \). These calculations were also made to evaluate the Doppler in relation to PSA rate, the degree of cellular differentiation, and in the diagnosis of extraprostatic extension. The MacNemar test was used when two methods were compared (significance threshold 0.05).

Results

Overall results of power Doppler after the series of initial and additional biopsies (table I)

Of the 579 patients explored, an anomaly was present on ultrasound and/or Doppler in 335 cases: in 260 cases, after the pathological examination, this anomaly corresponded to a cancer (260 true positives and 75 false positives). In the 244 other cases, where no anomaly was detected on power Doppler examination, we found 39 cancers and five PINs (prostatic intraepithelial neoplasia) (205 true negatives and 39 false negatives) (sensitivity [Se] 87%, specificity [Spe]: 73%, positive predictive value [PPV]: 78%, and negative predictive value [NPV]: 84%). The NPVs calculated for each group of patients classified by PSA level showed no statistically significant difference between them \( (p<0.01) \) (fig. 8); 83% of the total series of 299 cancers presented signs of hypervascularization on PDS. Of the 260 cancers declared true positives after PDS, we found hypoechoic and avascular lesions (ten cases) (fig. 9), isoechoic and hypervascular lesions (six cases) (fig. 5), and hypoechoic lesions vasularized by normal blood vessels (96 cases) (fig. 1 and 4) or abnormal vessels (89 cases) (fig. 1 and 6). In 59 cases, blood vessels originating in the tumor broke through the capsule (fig. 7d).

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Of patients with a Gleason score greater than or equal to 7, 69% presented abnormal vessels versus only 31% of patients with a Gleason score under 7. The presence of abnormal vessels was significantly correlated with the degree of the lesion’s cellular differentiation (p<0.01). The initial biopsies that were not PDS-guided diagnosed 214 cancers (186 true positives, 28 false negatives) and confirmed the diagnosis of 90.5% of the palpable tumors but missed 28.5% of the cancers. The complementary Doppler-guided biopsies diagnosed 85 cancers in the 141 patients who retained a pathological PSA level 6 months after the initial biopsies (74 true positives, 11 false negatives, 41 true negatives, 15 false positives; Se, 87%; Spe, 73%; PPV, 83%; NPV, 79%). Of the 74 cancers that presented a PDS abnormality diagnosed on the additional biopsies, 41% had a single positive biopsy with 13% exclusive anterior localization versus 25% and 6%, respectively, of the 186 true positives of the first series of biopsies (p<0.01 and p=0.04, respectively).

Fig. 1: Peripheral hypoechoic nodule of median sextant with normal hypertrophic vessels (PSA: 20 ng/ml, Gleason score: 5, positive biopsies in the three right sextants and one left sextant). No extraprostatic extension.

Fig. 1: Nodule hypoéchogène périphérique du sextant médian droit avec hypertrophie de vaisseaux normaux (PSA : 20 ng/ml, biopsies positives au niveau des trois sextant droits et d’un sextant gauche, score de Gleason : 5). Pas d’extension extra prostatique après prostatectomie radicale.

Fig. 1: Hypoechoic nodule of left basal sextant with abnormal vessels: the first sextant biopsies were negative (PSA: 8.6 ng/ml, one positive biopsy after repeat biopsies, Gleason score: 7). Extraprostatic extension after radical prostatectomy.

Fig. 1: Nodule du sextant basal gauche hypoéchogène avec vaisseaux anormaux ; première série de biopsies négatives (PSA : 8,6 ng/ml, 1 biopsie positive sur la deuxième série de biopsies, score de Gleason : 7). Extension extra prostatique après prostatectomie radicale.

Fig. 3: Focal lesion with power Doppler: small hypoechoic hypervascular peripheral lesion. (PSA: 5 ng/ml, one positive biopsy in left median sextant, Gleason score: 7). Focal lesion without extraprostatic extension after radical prostatectomy.

Fig. 3: Lésion focale à l’EDP : lésion hypoéchogène périphérique gauche de petite taille hyper vascularisée. (PSA : 5 ng/ml, sextant médian gauche positif à la biopsie, score de Gleason : 7, foyer lésionnel sans signe d’extension extra prostatique après prostatectomie).

Fig. 4: Hypoechoic edging of the entire peripheral prostate. (PSA: 5.5 ng/ml, six positive biopsies with 4-8mm of cancer, Gleason score: 6). No extraprostatic extension.

Fig. 4: Liseré hypoéchogène faiblement vascularisé de l’ensemble de la prostate périphérique en rapport avec une tumeur infiltrante. (PSA : 5,5 ng/ml, 6 biopsies toutes partiellement infiltrées, score de Gleason : 6) Pas d’extension extra prostatique après prostatectomie radicale.
Results of PDS after 107 radical prostatectomies (tables II and III)

The ultrasound image completely correlated with the result of the radical prostatectomy in 43% of the operated patients, partially correlated in 35%, and was discordant in 22%. The partially correlated cases were related to multifocal cancers. The discordant cases corresponded to false negatives (20 cases) and to cases where the lesion was found outside the suspected zone on PDS (four cases). Of the 20 operated patients with false-negative results, 11 lesions could be considered insignificant; inversely, no insignificant lesion was found in cases with a lesion visible on PDS (fig. 1).

Seventeen percent of hypovascular lesions, 25% of slightly vascularized lesions, and 38% of lesions presenting abnormal vessels were accompanied by an extraprostatic extension. When a blood vessel involved in the lesion broke into the capsule, a prostatic extension was present in 71% of cases (fig. 3). The existence or absence of intraslesional vascularization or the presence of normal or abnormal vessels did not provide a significant prediction of the risk of extraprostatic extension (EPE): the presence of blood vessels originating in the tumor that broke into the capsule seemed, like the PDS appearance, to be the most relevant for suspecting EPE (Se, 37.5%; Spe, 93%; PPV, 71%; NPV 78%) (p<0.0001).

Seventeen lesions were small on the Doppler (focus) or only slightly visible (subtle lesion): an extraprostatic lesion was present in four cases (2%). In contrast, 18 extraprostatic extensions were present in the 42 infiltrating or multifocal lesions (43%) (fig. 3).

An unexpected progressive aspect concerned three small tumors (focal lesion on PDS with a single positive biopsy) in the subcapsular position: radical prostatecto-
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Fig. 7: After staging, two lesions with the same forecast where Power Doppler Sonography (PDS) gave more information.

a-b: PDS result was negative: insignificant focal lesion after radical prostatectomy. (Over treatment?) (PSA: 5.4ng/ml, Gleason: 6.1 positive biopsy with 3mm of cancer).

c-d: With PDS, apical lesion with one vessel crossing the capsule behind the lesion: extraprostatic extension after radical prostatectomy. (PSA: 4.6ng/ml, Gleason 6.1 positive biopsy with 5mm of cancer).

Fig. 7: Deux lésions de gravité identique après le bilan initial (même taux sérique de PSA, même score de Gleason et même nombre de biopsies positives)

a-b: Lésion du sextant médian droit isoechogène et avasculaire (faux négatif de l’Echo Doppler Puissance) : après prostatectomie radicale petit foyer unique insignifiant. (PSA) : 5,4 ng/ml, Gleason 6,1 biopsie positive).

c-d: Lésion apicale hypoéchogène avec vaisseaux franchissant la capsule : après prostatectomie radicale extension extra prostatique. (PSA : 4,6 ng/ml, score de Gleason 6,1 biopsie positive).

Fig. 8: Results of negative predictive value after two series of biopsies according to variation in PSA level from 3.5 to 20ng/ml: no significant statistical difference was observed.

Fig. 8: Résultats de la VPN de l’écho Doppler puissance après 2 séries de biopsies prostatiques en fonction de la progression du taux sérique de PSA de 3,5 à 20 ng/ml : aucune différence statistiquement significative n’a été observée entre les différentes valeurs.

Fig. 9: Anterior nodular hypovascular cancer: hypoechoic nodule of right basal sextant without visible vessels (PSA: 9ng/ml, two right positive sextants after biopsies, Gleason score: 5). No extraprostatic extension.

Fig. 9: Cancer nodulaire hypovasculaire antérieure : lésion hypoéchogène du sextant basal droit sans vaisseau intra lésionnel visible. (PSA : 9 ng/ml, 2 sextants droits positifs aux biopsies, score de Gleason : 5, pas d’extension extra prostatique après prostatectomie).
but in two cases, perineural invasion was
present, demonstrating that they were likely to progress. Of the four patients with a Gleason score of 7, two extraprostatic extensions were found (one anterior tumor and one basal tumor in two patients whose prostate volume was greater than 60 cm³).
In cases of established cancer with a Gleason score less than or equal to 6 with a negative PDS result, the risk of having insignificant cancer (11/16 cases) was higher than the risk of having a lesion presenting signs of being aggressive (2/16 cases) (p<0.01).

**Discussion**

**The discriminating role of PDS in choosing which lesions to treat**

The diagnosis of prostate cancer is suspected based on a high serum PSA level and confirmed by biopsies. The threshold value usually retained – a serum PSA level of 4 ng/ml (10) is nonspecific and its sensitivity is far from perfect since 15.2% of cancers are reported to be found in subjects with serum PSA levels less than 4 ng/ml and 14.9% of lesions presenting a Gleason score greater than or equal to 7 (30). In our study, the percentage of lesions that were potentially aggressive found among a series of 39 patients presenting a nonpalpable and invisible cancer on PDS examination was 10%, whereas the mean serum PSA level was 11.46 ng/ml. The sensitivity of biopsies is itself difficult to evaluate because the biopsies sometimes miss their target, which has led to an increase in the number of biopsies (28.5% of undiagnosed cancers of the first biopsies in our study). Early diagnosis induced by screening with the PSA dosage is the cause of a bias making it difficult to evaluate the true gain in terms of years of life gained and a reduction in the mortality rate: for Draisma et al. (5), regular screening advances the initial diagnosis by a mean of 10 years (12.3 years at 55 years of age and 6 years at 75 years of age), 50% of cancers between 70 and 75 years of age, and a mean of two cancers out of three would never have been diagnosed and treated without screening. Screening may be the cause of over-diagnosis and overtreatment of small cancers said to be insignificant (27); the latter are sometimes not found on specimens of radical prostatectomy and this lack of histological confirmation can lead to litigious action: three cases in our series and two cases in the Cornud et al. study (24). For these reasons, screening using an isolated biological marker associated with biopsies taken systematically induces pernicious effects: PDS imaging is easy to implement and inexpensive compared to cancer treatment: at its best it can complete the work-up before treatment decisions are made.

When prostate cancer is established, the prognosis and therapeutic orientations depend on a statistical evaluation of the risk of distant recurrence after treatment (12) or the risk of extraprostatic extension (31). This does not take into account the lesion’s location, the size of the tumor focus, or the type of lesion (focal, nodular, infiltrating, multifocal). Two cancers with the same serum PSA level, the same Gleason score, and the same number of positive biopsies are considered to be identical, when the situation may be very different (fig. 7).

The positive, and particularly negative, predictive values of PDS in terms of PSA level progression show that the existence of a PDS image is correlated with the risk of cancer and not with how high the PSA

### Table III

Comparison after radical prostatectomy (PR) in 107 patients between vascular and echographic findings with power Doppler sonography with mean PSA level, mean Gleason score, and number of extraprostatic extensions.

<table>
<thead>
<tr>
<th>Vascularization</th>
<th>Number of PR</th>
<th>Mean PSA (ng/ml)</th>
<th>Mean Gleason score</th>
<th>Extraprostatic extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not seen</td>
<td>20</td>
<td>11.46</td>
<td>5.37</td>
<td>2/20 (10%)</td>
</tr>
<tr>
<td>Focal</td>
<td>12</td>
<td>7.14</td>
<td>5.69</td>
<td>3/12 (25%)</td>
</tr>
<tr>
<td>Nodular</td>
<td>28</td>
<td>10.56</td>
<td>6.57</td>
<td>8/28 (28%)</td>
</tr>
<tr>
<td>Infiltrating</td>
<td>33</td>
<td>15.32</td>
<td>6.34</td>
<td>14/33 (42%)</td>
</tr>
<tr>
<td>Multifocal</td>
<td>9</td>
<td>9.03</td>
<td>6.28</td>
<td>4/9 (44%)</td>
</tr>
<tr>
<td>Subtle</td>
<td>5</td>
<td>12.12</td>
<td>5.5</td>
<td>1/5 (20%)</td>
</tr>
</tbody>
</table>

### Table III

Comparison after radical prostatectomy (PR) in 107 patients between vascular and echographic findings with power Doppler sonography with mean PSA level, mean Gleason score, and number of extraprostatic extensions.

<table>
<thead>
<tr>
<th>Echographic aspect</th>
<th>Number of PR</th>
<th>Mean PSA (ng/ml)</th>
<th>Mean Gleason score</th>
<th>Extraprostatic extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypo-or avascular nodule</td>
<td>6</td>
<td>15.7</td>
<td>5.6</td>
<td>1/6 (17%)</td>
</tr>
<tr>
<td>Accented normal vascularization</td>
<td>38</td>
<td>9.06</td>
<td>6.021</td>
<td>9/38 (25%)</td>
</tr>
<tr>
<td>Abnormal vascularization</td>
<td>21</td>
<td>14.07</td>
<td>6.33</td>
<td>8/21 (38%)</td>
</tr>
<tr>
<td>Extracapsular vessels</td>
<td>17</td>
<td>12.57</td>
<td>6.88</td>
<td>12/17 (71%)</td>
</tr>
<tr>
<td>Abnormal vascularization with no nodule</td>
<td>5</td>
<td>9.15</td>
<td>5.330</td>
<td></td>
</tr>
</tbody>
</table>
rate is. Other studies have shown the strong negative predictive value of PDS (Remzi et al. using PDS to perform the first and second series of biopsies found negative predictive values higher than ours: 87.9% and 94.4% versus 84% and 78%, respectively) (32). Other studies have found negative predictive values for power Doppler varying between 86% for Halpern and Strup (22) and up to 99% for Okihara et al. (33).

In our study, the correlation of the PDS image and the results of radical prostatectomy was total in 43% of cases, partial in 35% of cases (notably in multifocal cancers), and absent or discordant in the other cases. Visualizing the lesion by ultrasound means demonstrating modifications in the intraprostatic ecostructure: high-grade lesions were the most visible and presented the highest number of abnormal blood vessels and the lowest number of false negatives. Our study confirms Cornud et al.’s (24), which noted that none of the patients with hypervascular cancer presented an insignificant cancer and that hypovascular and invisible cancers were those that presented the lowest risk of progression. For Halpern and Strup (22), PDS was not advantageous because it could not visualize all the lesions corresponding to each biopsy in a particular patient: this was also true for us since total concordance was only observed in 43% of cases after radical prostatectomy, but PDS was able to identify the main lesion in 78% of cases. A relation between vascularization on the PDS image and the seriousness of a lesion should be compared to the observations in immunohistochemical studies on angiogenesis (34, 35) or stroma reaction (36). Indeed, in prostate cancer the stroma microenvironment seems to be altered compared to normal stroma, with signs of repair occurring on this stroma, given that the stroma reaction is made up of stimulated myofibroblasts and fibroblasts and evolves with cancer progression. It replaces the normal fibromuscular stroma. A significantly greater proportion of myofibroblasts is found in grade 4 cancers than in grade 3 cancers. PDS also shows ecostructure and vascularization differences depending on tumor grade. This may mean that a tumor visible on ultrasound (hypoechogenic zone) has a stroma reaction that is already organized; its vascularization may be an indirect sign of angiogenesis that would intensify as the tissue dedifferentiation increases; often only the main lesion focal is visible among the frequent multifocal tumors (35% in our study). If the number of diagnosed cancers must be limited only to those that are potentially aggressive, power Doppler sonography seems to provide good results in discriminating tumors that also have a stroma reaction and/or evolved angiogenesis.

T1c-stage and insignificant cancers
Insignificant or latent cancers (27) are cancers that do not progress sufficiently to have a deleterious effect on duration or quality of life: they are generally nonpalpable T1c-stage cancers with a Gleason score less than 7. Their volume is less than 0.5 cc, but this last datum is difficult to determine before intervention, because a small cancer focus on a single biopsy is not a guarantee of a clinically insignificant tumor (37). Stage T1c groups a heterogeneous population of tumors with a differing potential to evolve, and of these, during radical prostatectomies only 25% concerned cancers that were potentially insignificant (27). This study brings up an interesting correspondence between false-negative imaging results, the biopsies, and the prostatectomy results: of the 107 patients who had a radical prostatectomy, 20 PDS false negatives were classed T1c; 15 of these cancers with a Gleason score less than or equal to 3 were considered insignificant after the biopsies. Eleven intraprostatic cancers after intervention indeed corresponded to low-volume lesions and were considered insignificant (10% of all radical prostatectomies). The lesions classed T1c after a negative PDS seemed to correspond to weakly aggressive lesions. The combination of a PDS false-negative result, a single positive biopsy, and a Gleason score less than or equal to 3 could be an indication for delaying aggressive treatment in the oldest patients or in those who wish to preserve their quality of life first and foremost.

Biopsies
The systematic increase in the number of biopsies may be the cause of certain problems such as:
- the diagnosis of a higher number of nonsignificant micro-cancers (38).
- an increase in the risk of infection and hemorrhage, even if they remain acceptable (7).
- Finally, the risk of seeding that is usually considered to be zero. However, some authors (39) have shown that prostatic cells are disseminated in the circulation after biopsies, which could contribute to distant metastasis. These same authors indicated that other studies would be necessary to confirm their observation. In the present study, three subcapsular cancer foci in which the capsule was inevitably transfixed and weakened during diagnosis unexpectedly presented an extraprostatic extension in the lesion area: could the secondary hemorrhage at the puncture site have prompted this extension?

The biopsy protocol used in the present study depended on the organization of the urology and medical imaging departments. The 12 initial biopsies that are currently recommended (six classical and six more lateral) were taken, but at two distinct times, the second only necessary in 24% of the cases investigated. When there was a clinically palpable cancer, the first six biopsies were sufficient in 90.5% of the cases at initial diagnosis. In small, nonpalpable but visible lesions, PDS guidance would have made it possible to limit the overall number of biopsies from the first series by immediately directing the sampling toward the most aggressive foci. The indication for a protocol with a higher number of biopsies could be limited to patients with an abnormal serum PSA level with no palpable or visible lesion on PDS (T1c), who would have chosen the security of an early diagnosis; they would be exposed to overtreatment in case of latent cancer diagnosed fortuitously (11/20 T1c patients after PDS were operated on in our series). Patients classed T1c after PDS could also be proposed additional exploration before biopsies such as MRI with dynamic injection of contrast product or endoluminal ultrasound using a contrast agent.

Conclusion
The absence of insignificant lesions among the visible tumors, its high negative predictive value, independent of the serum PSA level in the search for tumors (84%), the presence of abnormal intrale-
sional blood vessels significantly higher in lesions that are not well differentiated, the risk of extraprostatic extension in cases of tumor vessels breaking into the capsule (71%) all make PDS a high-performance technique. It also provides precise ultrasound guidance for a limited number of biopsies, and it can contribute to presuming that certain lesions classified T1c after PDS are insignificant and belong to a group of cancers that are less serious. Even though our results should be nuanced and confirmed by other research teams, this currently optional technique can contribute useful information to the oncologist-clinician and the urologist, and therefore seems necessary to good management of patients with prostate cancer.

References


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