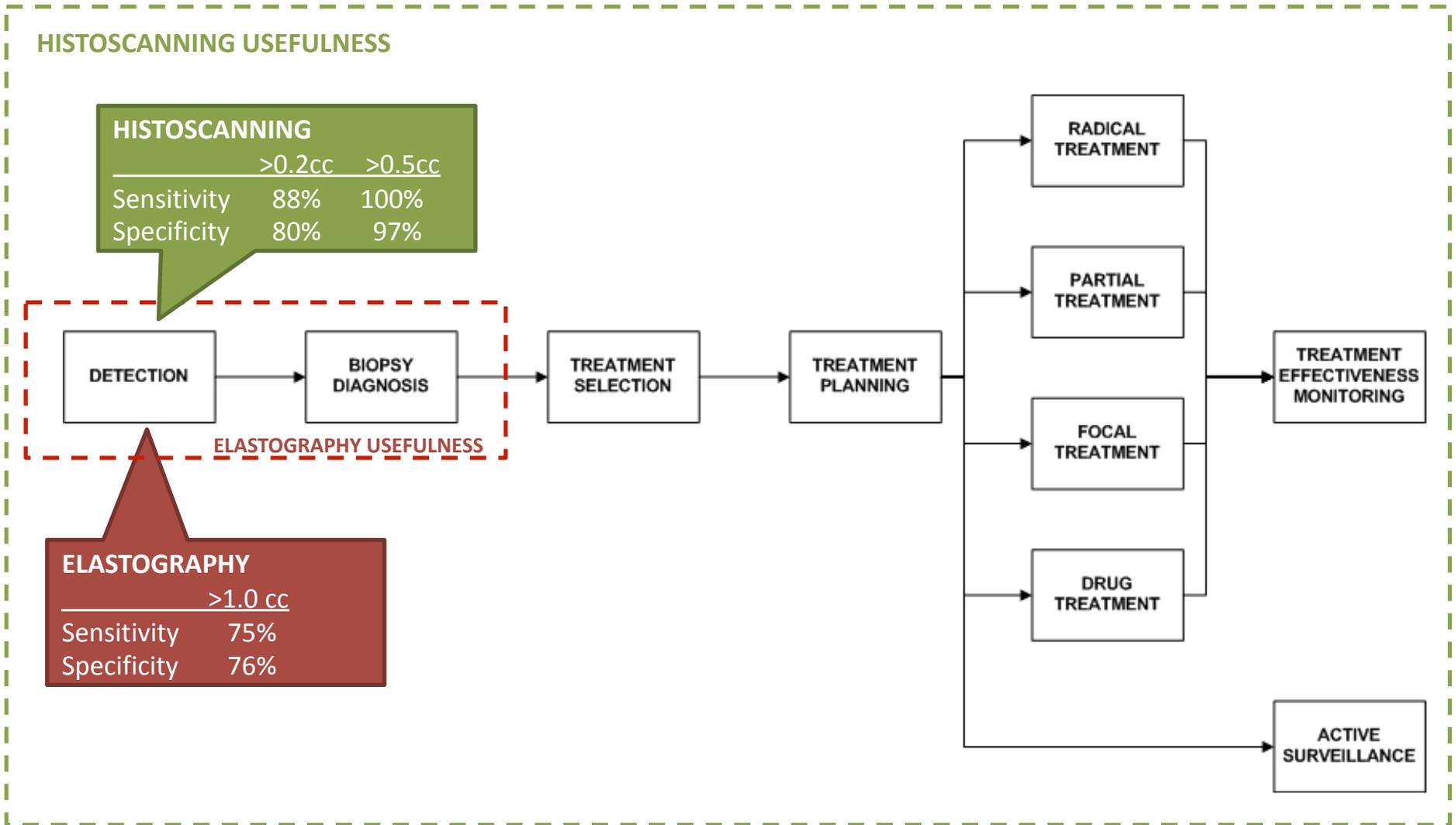


Positioning of prostate HistoScanning

Create value along the entire patient pathway *with emphasis on treatment.*



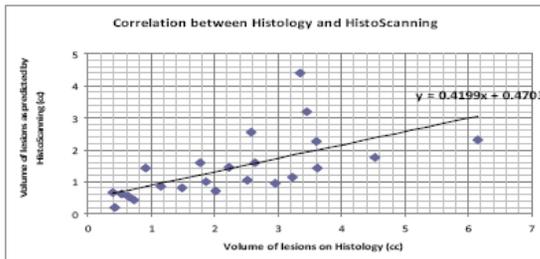
HistoScanning results presented at BAUS 2009

Volume threshold for detection	≥ 0.20 cc	≥ 0.50 cc
Sensitivity	88 %	100 %
Specificity	80 %	97 %
Positive Predictive Value	72 %	91 %
Negative Predictive Value	92 %	100 %

ELASTOGRAPHY

> 1.0 cc
75%
76%
87%
59%

Salomon 2008: Sensitivity and specificity were about 76%, the positive predictive value was 87%, and the negative predictive value was about 59%



Graph 1: Correlation between the histological estimation and HistoScanning prediction of volume of lesions above 0.2 cc (Spearman Correlation Co-efficient $r = 0.8$, $p < 0.001$, highly significant).

No such data available for Elastography

Pathway stage & Clinical requirement	Requirements	HistoScanning	Elastography																									
Detection (Screening) <i>No significant cancers missed, few false positives</i>	High Sensitivity and specificity at 0.2 cc or 0.5 cc cut-off. Robustness of the method (no interoperator variability)	<table border="1"> <thead> <tr> <th></th> <th>0.2cc</th> <th>0.5cc</th> </tr> </thead> <tbody> <tr> <td>Sensitivity</td> <td>88%</td> <td>100%</td> </tr> <tr> <td>Specificity</td> <td>80%</td> <td>97%</td> </tr> <tr> <td>PPV</td> <td>72%</td> <td>91%</td> </tr> <tr> <td>NPV</td> <td>92%</td> <td>100%</td> </tr> </tbody> </table>		0.2cc	0.5cc	Sensitivity	88%	100%	Specificity	80%	97%	PPV	72%	91%	NPV	92%	100%	<table border="1"> <thead> <tr> <th></th> <th>>1.0 cc</th> </tr> </thead> <tbody> <tr> <td>Sensitivity</td> <td>75%</td> </tr> <tr> <td>Specificity</td> <td>76%</td> </tr> <tr> <td>PPV</td> <td>87%</td> </tr> <tr> <td>NPV</td> <td>59%</td> </tr> </tbody> </table>		>1.0 cc	Sensitivity	75%	Specificity	76%	PPV	87%	NPV	59%
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Biopsy diagnosis <i>Accurate targeting of biopsy towards lesions.</i>	<u>Real time</u> (RT) guidance capability Accurate size and location matching	Accurate location and size (r=0.8, p<0.001) determination. (Kumar, Emberton, BAUS 2009) Investigator initiated study: ERASMUS Rotterdam, Biopsy yield.	No known studies about size and location measurement																									
Treatment selection <i>Correct grading and staging of the PCa.</i>	Accurate determination of size, location, focality, laterality, EPE. Accurate Gleason grading.	Accurate location and size (r=0.8, p<0.001) determination. (Kumar, Emberton, BAUS 2009) Reliable Gleason grading only by biopsies.	No known studies about size and location measurement																									
Treatment planning <i>Proximity of PCa to critical structures (nerves, urethra, capsule) allowing appropriate treatment margins.</i>	Accurate determination of size, location, focality, laterality, EPE. Accurate determination of lesion margins	Accurate location and size (r=0.8, p<0.001) determination. (Kumar, Emberton, BAUS 2009) Reliable Gleason grading only by biopsies.	No known studies about size and location measurement																									
Treatment support (during procedure)																												
<ul style="list-style-type: none"> Prostatectomy 	Intra-operative accurate determination of lesion margins.	No role <u>during</u> surgery only in planning the surgery.	No role during surgery																									
<ul style="list-style-type: none"> Focal (Brachy, HiFu, Cryo) <i>Real time treatment guidance.</i> <i>Verification that all diseased tissue was treated.</i> 	Accurate determination of size, location, focality, laterality, EPE. Accurate determination of lesion margins. Intra procedural testing of remaining positive tissue. Results not affected by applied treatment.	Accurate focality, laterality and size (r=0.8, p<0.001) determination. (Braeckman et al BJUI 2007, 2008; Kumar, Emberton, BAUS 2009) Preliminary tests of HistoScanning pre- peri- and post Brachy very encouraging. Several investigator initiated studies underway. (Langley, Emberton)	No role during focal treatment																									
Treatment effectiveness monitoring <i>For each identified lesions determine evolution of size and grade.</i>	High Sensitivity and specificity at 0.2 cc Repeatability of size and location measurements. Facilitate follow-up to follow-up comparisons. Ability to differentiate between diseased tissue and effectively treated tissue. (eg. necrosis)	Accurate focality, laterality and size (r=0.8, p<0.001) determination. (Braeckman et al BJUI 2007, 2008; Kumar, Emberton, BAUS 2009)	No available evidence																									

Pallwein et. al. BJUI 2007: "RTE detected 28 of 35 cancer foci (>0.5cc) (sensitivity 80%). Seven foci were not detected with RTE and 3 were in the inner gland. "RTE has shown promise in detection of breast and thyroid lesions. However, limitations noted in the prostate include an increase in stiffness due to chronic inflammatory tissue, BPH, and small (<0.5 cc) lesions. "

Dr Georg Salomon, European Hospital 2008: We compared pre-surgery ultrasound data of cancer patients with the post-surgical histological results of the removed tissue. Sensitivity and specificity were about **76%**, the positive predicative value was **87%**, and the negative predictive value was about **59%**.

Tsutsumi, Masakazu et al, International Journal of Clinical Oncology, Volume 12, Number 4, August 2007 , pp. 250-255(6)

In 15 patients (29%), all EMIs were in complete agreement with tumor location (category I), in 28 patients (55%), the EMIs agreed with tumor location, but showed some disagreement (category II), and in 8 patients (16%) there was disagreement of the elastographic findings with tumor location or the tumors were undetectable by elastography (category III). However, in category III, all tumors were detected as low-echoic by B-mode ultrasonography. We divided the prostate into three different regions (anterior, middle, and posterior), and found that 30/32 (94%) anterior tumors, 13/17 (76%) middle tumors, and 16/28 (57%) posterior tumors were detected by elastography.

Masahiro Sumura et al, International Journal of Urology Volume 14 Issue 9, Pages 811 - 816

"cancer detection rate with real-time elastography was superior to the rates of other modalities and nearly equal to both on the anterior side (75.0%) and the posterior side (73.7%) of the prostate. "

Dr. Douglas Chin, Arcadia California: "This modality is not for everyone because **success with it is so heavily dependent on the skills of the operator,**" he explains. "It requires someone who is very knowledgeable about elastography and mechanically adroit with it, because how you vary the pressure and the angle of the probe can affect the accuracy of the measurement of elasticity. Consequently, pressure and angle must be consistent throughout the duration of the exam."