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Prospective phase I trial of differential dose prostate brachytherapy guided by cancer-specific tissue-type imaging (TTI) and ultrasound spectrum analysis (USA): Preliminary dosimetric and clinical results

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Introduction: Standard prostate cancer treatments treat the entire gland uniformly, and many focal treatments treat only the dominant tumor, ignoring small foci of cancer. We propose an alternative approach where tumor areas are treated with a higher dose of radiotherapy and the remainder of the prostate with a lower dose. Tissue-type images (TTIs) based on ultrasound spectrum analysis (USA) analyze the spectra of radiofrequency ultrasound echo signals to identify intraprostatic tumor and have been shown to correlate with biopsy findings. We conducted a phase-I prospective trial to evaluate the safety and technical capability of using TTIs to guide differential dose low dose-rate prostate brachytherapy.

Methods: 14 low risk patients were enrolled. Standard B-mode ultrasound (Figure 1) and TTIs (Figure 2) were generated intraoperatively and images were fused. Based on TTIs, plans were developed to deliver 200% prescription dose to the tumors and 100% to the prostate (Figure 3). Doses above 100% to non-tumor regions were minimized, and standard normal tissue constraints were respected. For comparative purposes, a standard plan, without knowledge of the tumor locations also was created (Figure 4).

Results: 12 patients had the procedure performed successfully. In one patient, technical problems occurred, and one patient had the procedure abandoned due to discordance of TTIs with MRI and biopsy findings. Tumor dose was significantly higher in TTI-based plans, mean tumor V200%: TTI vs. standard 97% vs. 48%, $p<0.05$. Modest dose reduction of prostate outside tumors also was achieved with TTI-based plans: TTI vs. standard: V100% (97% vs. 99%, $p<0.05$), V150% (61% vs.74%, $p<0.05$), V200% (37% vs.41%, $p<0.05$). The follow-up range was 4 to 30 months, median 10.5 months. A low incidence of grade 2 side effects was observed (Table 1) and no grade 3-4 toxicities were seen. Disease free survival was 100%.

Conclusions: Differential dose prostate brachytherapy using TTI guidance is technically feasible with low toxicity. Additional patients and longer follow-ups are needed to confirm the safety and efficacy of this approach.

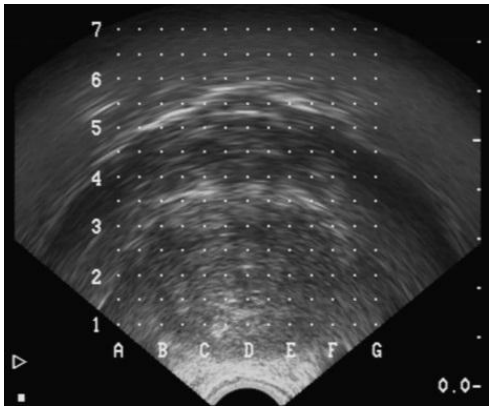

Figure 1

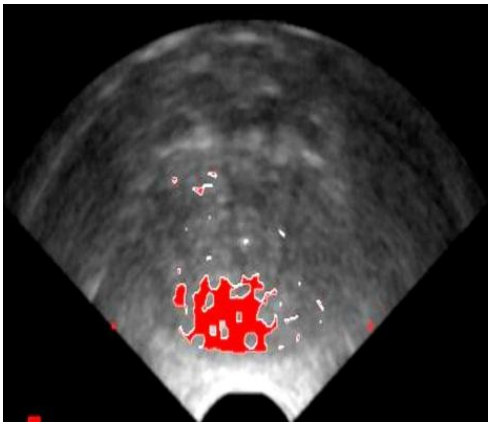

Figure 2

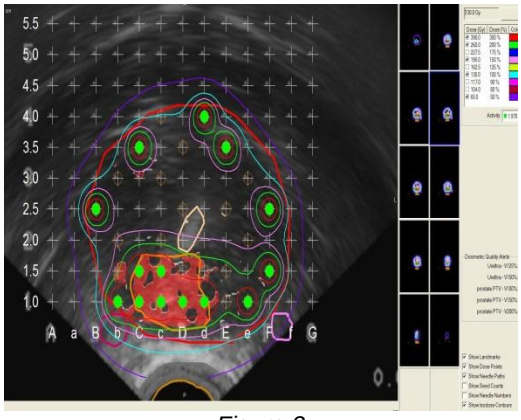

Figure 3

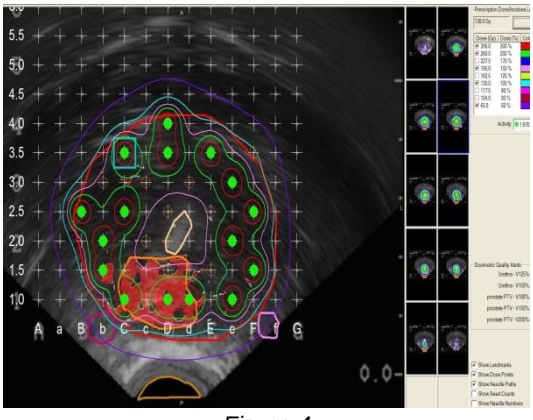

Figure 4

Table 1. Number of Patients with Grade 2 or Higher Toxicity

	Acute			Late		
	Grade 2	Grade 3	Grade 4	Grade 2	Grade 3	Grade 4
Sexual	7	0	0	4	0	0
Urinary	7	0	0	4	0	0
Rectal	0	0	0	1	0	0

* Acute: ≤ 3 months since procedure, Late: > 3 months since procedure