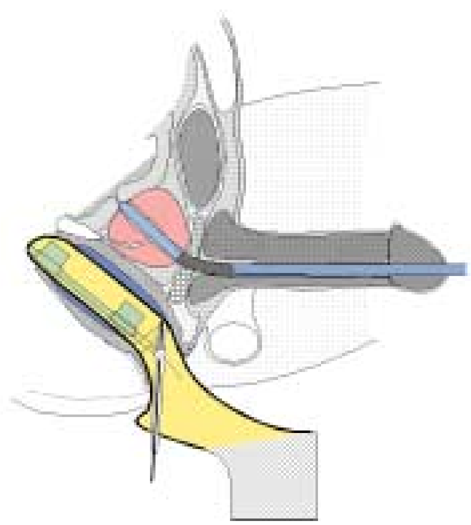
Prostate Cancer Detection/Analysis/Mapping System

The goal of our work is to develop dramatically improved detection, analysis and mapping of prostate cancer using an integrated package of ultrasound technologies, and then to provide immediate, effective and minimally-invasive treatments for early stage (small) tumors. In partnership with SMTS Corporation, a local startup, we are developing and testing a family of advanced ultrasonic technologies detection of prostate cancer. The prototypes we have built are being used in a clinical human patient testing program at Walter Reed Army Medical Center (WRAMC) in Washington, DC.



Although ultrasound is used in various ways during a patient's encounter with prostate cancer, to date there are no fully integrated systems that are optimized for this application. Moreover, there are a large number of emerging technologies that can be brought together in a synergetic manner to provide for a big advance in the detection and treatment of this most diagnosed cancer in American men. The foundation of the SMTS system is well-proven ultrasound, but used in a fundamentally different way: 3D ultrasound *plus* automatic interpretation *plus* robotic biopsy of suspicious areas. The heart of the system is shown at the left, with computer-controlled scanning ultrasound both from the rectum (trans-rectal probe shown in yellow) and from inside the prostate itself (trans-urethral catheter probe shown in blue). Dual probes allow higher ultrasonic frequencies for much better resolution, and computer control allows the scans to be absolutely registered for treatment as well as repeat scanning to track changes over time.

Prototype I (shown at right) was delivered to WRAMC at the conclusion of Phase I of this project, so that volunteers could be scanned ultrasonically before radical prostatectomy. Comparison of the ultrasonic data sets with the gold standard of pathology is the key to teaching the software expert system to *automatically* determine level of suspicion for cancer. In use, the physician master instructs the robotic slaved-biopsy subsystem to extract tissue samples from indicated suspicious regions to confirm malignancy. The rapid and highly accurate biopsy mechanism is integrated into the system, which is rigidly attached to a special chair for absolute registration with the ultrasound scanning system.

At the start of Phase II two laboratory apparatus were constructed at William and Mary to work in parallel with the clinical testing program. Aa sophisticated "mockup" of the

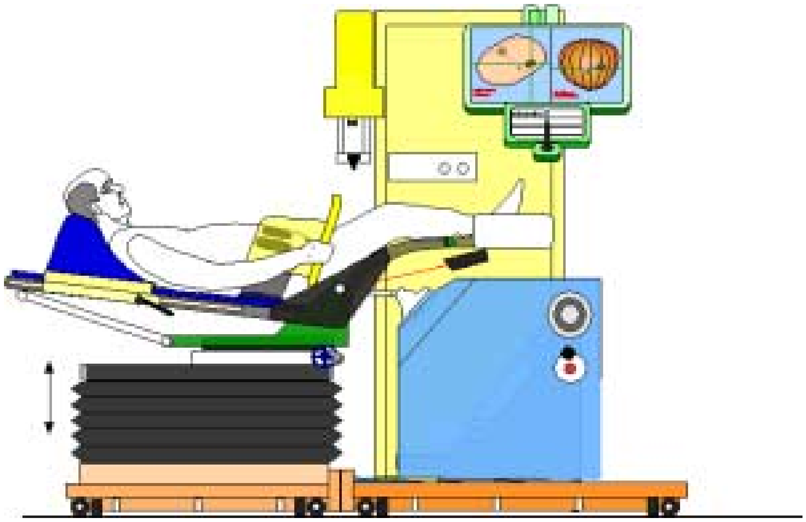
clinical prototype was designed and fabricated with identical computer, ultrasonics and custom-built motion control hardware and software to that of Prototype I. The open architecture of this system (shown at left above) allows numerous modifications and upgrades to be fully checked out before installing them on the clinical system. It also allows phantom and in vitro data to be acquired easily. At the Applied Research Center, where SMTS and W&M are co-located, another laboratory facility (shown at right above) was also established. The work being done there is focused on developing 4D high-resolution Doppler, dynamic elastography, and other advanced ultrasonic techniques that will be incorporated into the clinical systems in Phase III. In addition, computational facilities were established at both W&M and ARC to perform computer simulations (in numero experiments) as well as to develop the artificial intelligence software that is at the heart of the SMTS system. All of these facilities were built using the extensive infrastructure of Prof. Hinders' laboratories that was already in place, which allowed SMTS to avoid the significant expense of starting from scratch and allowed much more of the available funding to be devoted to active research and technology innovation than would otherwise have been possible.

4D High Resolution Doppler: Using the ARC laboratory facilities we have been developing an enhanced Doppler imaging technique, which will be incorporated into the clinical prototypes in Phase III. The ultrasonics and data acquisition portions of the ARC instrumentation is the same as in the clinical prototype, and work during the last year has been focused on developing and testing (with custom built apparatus and phantoms) the detailed algorithms that will enable the prototypes to do 4D Doppler imaging. Because the SMTS system is not a video-frame-rate imager, it is not restricted to the amount of information that can be displayed on a screen for interpretation by a human. Doppler is usually shown as a false-color overlay to B-mode images, but at low resolution and poor area coverage because of frame-update restrictions. We use Doppler as an additional input to the software expert system, so we are able to use the entire spectral Doppler signal at each point in the prostate volume. Moreover, we can sample the complete prostate volume at much higher resolution, and can process the signals to give color and power Doppler outputs. Doppler is important because cancer is associated with increased vascularity in the vicinity of the tumor. Mapping out the pattern of vascularity in the prostate can indicate potentially suspicious regions for biopsy.

Dynamic Elastography: Prostate cancer is stiffer than the surrounding tissues, which is why the digital rectal exam is an effective screening procedure for large tumors in the peripheral zone. Some cancers (isoechoic) do not show up on ultrasound images. However, elastography is a newly-emerging technique that allows tissue “stiffness” to be imaged using ultrasound. In most implementations, ultrasonic scans are performed before and after a slight compression of the tissues. Although the B-mode images will appear identical, computerized comparison of them allows the subtle motion of the speckles to be compared. Stiffer regions will compress less, and so by displaying the motion of the speckles an “elastogram” or stiffness image can be developed. Applying a static compression to the prostate is problematic. Our approach is to use an external vibration belt on the patient’s abdomen to compress dynamically the prostate, what we are calling dynamic elastography. This avoids the mechanical complication and discomfort of providing the compression via the trans-rectal probe. We then use the high-resolution Dopper system to track prostate vibrations, with the stiff tumors vibrating less than the healthy tissues. Work during Phase II has concentrated on developing and testing (using custom designed and built apparatus) the algorithms for dynamic elastography, as well as detailed conceptual design and preliminary evaluation of the external vibration belt using NASA’s new THUNDER piezo-actuators. We have also been developing the detailed sophisticated three-dimensional dynamical elasticity formalism that will enable the clinical use of the measured data. As with the Doppler data sets, the elastographic stiffness maps of the prostate volume will be passed to the software expert system as additional inputs to determine the level of suspicion for cancer throughout the prostate.

Software Expert System: As mentioned several times above, the heart of the SMTS system is software artificial intelligence that develops a level of suspicion (LOS) map for cancer throughout the prostate volume. Rather than depending on a human to search for suspect features in the images, the multiple ultrasonic, 4D Doppler, and elastography data sets are processed in the computer to make that preliminary determination. A false-color LOS map is then presented to the physician for selection of biopsy at those areas, which are likely cancer. The human testing protocol is designed to teach the expert system to recognize cancer by providing direct comparison to the pathology gold standard. Men whose prostates are already scheduled to be removed are first scanned with the SMTS system and the multiple ultrasonic data sets are recorded. Comparison to subsequent pathological findings allows the software to be “taught” which ultrasonic features correspond to cancer and which don’t. The first portion of the work involved developing robust and automatic algorithms that can identify the gross features of the prostate volume, which we call the “boundary outline” part of the problem. This work has been successful on phantom data, and we are especially eager for the flow of patient data to begin in order to refine and finalize these algorithms. We have also begun developing and refining algorithms based on the military target identification and tracking literature, as well as neural-network and wavelet-based schemes for developing the LOS mapping software.

Schematic of current design for Prototype II



The full capability of the SMTS system is realized via treatment in addition to diagnosis of prostate cancer. The same robotic biopsy system that accurately retrieves tissue samples for the pathologist, can also perform localized treatment of confirmed malignancies. During the Phase II effort we have performed preliminary design studies of a variety of treatment options, as well as additional in situ diagnostics, that can be incorporated into the slaved biopsy subsystem.

- *Brachytherapy Seed Implantation:* By replacing the biopsy needle tissue extraction mechanisms with seed implantation mechanisms, the same robotic system can be used to accurately place the radioactive pellets throughout the prostate, as well as to accommodate some new innovations in radioactive seed implant therapy.
- *Thermal Treatment Subsystem:* For early stage/small prostate cancer conditions, localized thermal ablation of confirmed tumors can be done by replacing the biopsy needle with an end-effected thermal subsystem that is inserted robotically directly into the center of the tissues to be destroyed. Alternatively, cryogenically freezing specific, localized volumes in the prostate can be accomplished with a variant of this treatment subsystem. In both cases, the progress of the treatment can be monitored in real time by scanning with the ultrasound probes to visualize the necrotic tissue zone.
- *Bio-impedance Imaging:* By putting a pair of small coils near the tip of a modified biopsy needle the bio-impedance of the tissue can be measured in situ. The complex "resistivity" of prostate tissues has been shown to differ in diagnostically useful ways for cancerous versus healthy tissues because of the differing cellular wall architecture. The SMTS system allows for this and other in situ diagnostic modalities to be added downstream.

These and other novel technologies will be explored in the planned Phase III effort.