Three-Dimensional Ultrasound Imaging System for

Prostate Cancer Diagnosis and Treatment

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Prostate cancer holds the second highest mortality rate among all cancers in men in North America, and is the most commonly diagnosed cancer in men [1]. Since the introduction of the prostate specific antigen (PSA) blood test for prostate cancer, diagnosed cases have increased dramatically, in fact, in 1995, there were 244,000 new cases and more than 40,000 deaths due to prostate cancer in the United States. It is believed that the prevalence of prostate cancer is high in 50 year-olds, with some 30% testing positive. However, many of these cancers remain asymptomatic until extensive local growth or metastasis of the tumor has occurred, or until the individual dies of some other disease.

Clinical assessment of the prostate gland is difficult due to its inaccessible location. In the past, this has been done by physical examination, prostatic fluid inspection, biopsy, or surgery. At present, the most commonly used screening techniques for prostate cancer are the digital rectal examination and the PSA test. Physicians widely use PSA testing for the diagnosis and monitoring of prostate cancer, and the test's role is well established. The level of PSA secreted by the prostate gland is measured in a simple blood test, and can signal the presence of prostate cancer in an asymptomatic man. In spite of its widespread use, applying PSA testing for the early detection and staging of prostate cancer remains controversial due to its less-than-ideal specificity. In an effort to improve the clinical utility of the PSA test, many investigators have attempted to increase its discriminating power by normalizing the PSA value with the prostate volume. It is generally believed that measuring the prostate and/or tumor volume is important in interpreting the PSA level. Until now, this task has been performed using transrectal ultrasound 2D imaging, although with less accuracy than clinically desirable.

Minimally Invasive Prostate Therapy

Revolutionizing surgery, minimally invasive procedures afford significant reductions in patient morbidity, recovery time, hospital stay, and overall cost, while preserving or increasing clinical efficacy. Clearly, a minimally invasive procedure for prostate cancer giving these benefits would be welcome, especially considering the significant morbidity currently associated with traditional therapies such as radical prostatectomy.

As a result, percutaneous ultrasound-guided prostate therapy techniques such as brachytherapy are currently under intense investigation. Although brachytherapy is capable of destroying tumors while preserving adjacent structures, the inconsistency in different institutions suggests that current practice is highly operator-dependent. From our past experience, it is clear that a major source of this variability is the standard use of conventional, hand-held 2D transrectal ultrasound (TRUS) for treatment planning, implantation guidance, and treatment monitoring.

Limitations of 2D TRUS

It is generally agreed that the conventional 2D TRUS examination is an important technique for imaging the prostate. However, conventional 2D TRUS has some serious limitations. They arise because only one thin slice of the patient can be viewed at any time, and the location of this image plane is controlled by physically manipulating the transducer orientation. Consequently:

- The surgeon must mentally integrate many 2D images in order to form an impression of the 3D anatomy and pathology. This process is not only time-consuming and inefficient, but more importantly, variable and subjective, possibly leading to incorrect decisions in diagnosis, planning, and delivery of the therapy.

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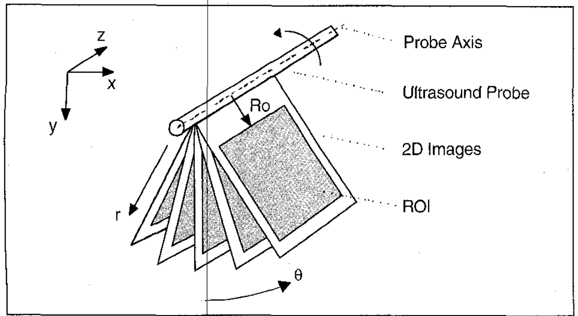

Fig. 1. This schematic diagram shows a side-firing, transrectal ultrasound transducer being rotated for a 3D imaging scan.

- It is difficult to place the 2D image plane at a particular location within an organ, and even more difficult to find the same location again at a later time. This makes 2D TRUS ill-suited for planning or monitoring therapeutic procedures.
- Due to the restrictions imposed by the patient's anatomy or position, sometimes it is impossible to orient the 2D TRUS transducer to the optimal image plane. This hinders the visualization process a during the therapeutic procedure.

Here, we describe our development of a 3D ultrasound imaging system that overcomes the limitations of conventional 2D TRUS. We describe the system and its operation, show images of patients, and report on the performance of this system. This includes the intra- and inter-observer variability of prostate volume estimation. Additionally, we show that volume estimation by the 3D ultrasound method is statistically significantly better than the conventional 2D method.

3D Image Acquisition

The 3D ultrasound system for imaging the prostate consists of three major components: an ultrasound machine with a transrectal ultrasound transducer; a microcomputer with a video frame-grabber; and a motorized assembly to rotate the transducer under computer control [2]-[6]. The microcomputer is also used for image reconstruction, display, and analysis of the 3D images.

Figure 1 shows the operating principles of our approach. The TRUS transducer is mounted in the assembly, and then covered with a water-filled condom. When the motor is activated, it rotates the transducer around its long axis. As the transducer is rotating, B-mode images are digitized and stored in the microcomputer. For a typical 3D scan, the transducer is rotated through about 80°, while 100 images are digitized at 15 images/s. After the rotation has been completed, the series of 2D images are reconstructed into a single 3D image. This new image is viewed on the microcomputer monitor and manipulated using interactive 3D visualization tools (Fig. 2)[2],[3].

Ultrasound System Performance

Distance Measurement

In reconstructing the 3D image, any inconsistencies may result in image distortions, in turn, yielding erroneous distance measurements. We evaluated the accuracy of distance measurements by imaging a 3D wire phantom of known dimensions, then measured the distances between the wires. The phantom comprised four layers of 0.25-mm diameter surgical wires, with eight parallel wires per layer. Each layer and every wire were separated from their neighbors by 10.00 mm. The wire phantom was immersed in a 7% glycerol solution, and then imaged with the 3D system.

The wire phantom was scanned first with the wires placed parallel to the probe's axis of rotation, then with the wires oriented parallel to the x axis. Nine 3D scans were performed in each case, with the phantom positioned at different distances from the transducer. The 3D images were reconstructed using 100 2D images, which were collected over 60°. The mean separations between adjacent wires showed that the 3D TRUS system had an error in distance measurements of about 1.0%.

Volume Measurement in 3D Images of Balloons

An important application of 3D prostate imaging is for normalizing the PSA value with the prostate volume. To evaluate the accuracy of volume measurements using the 3D TRUS approach, we imaged five balloons filled with different known volumes of 7% glycerol solution, and compared the measured volumes obtained from the 3D images to the true volumes. Each image data set consisted of 100 2D images, scanned through 60°.

To obtain the volume of each balloon, each 3D image was "sliced" 0.2 mm apart to produce successive 2D image planes. For each 2D image, the balloon boundary was then manually outlined, and the number of pixels within the boundary determined. Multiplying the sum of the total number of voxels within all the boundaries by the voxel volume yielded the

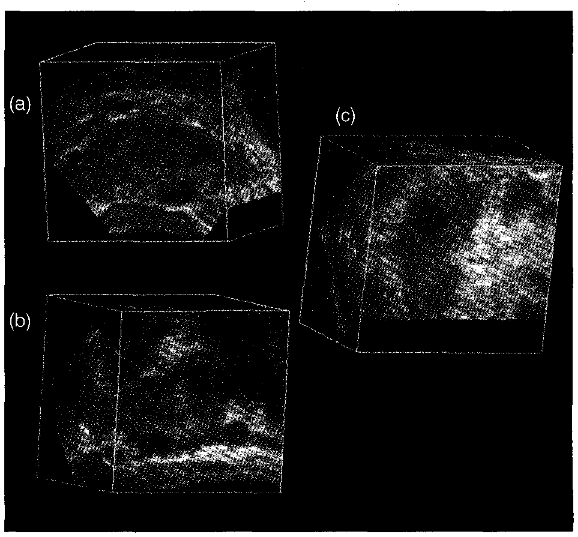

Fig. 2. At view here are 3D ultrasound images showing a prostate with a tumor. The volume is "sliced" by planes that can be angled and positioned interactively by the user to obtain the desired view. The prostate image has been "cut" in the transaxial plane to reveal the tumor as a hypoechoic region, located just above the periprostatic fat region (a). By slicing the image parasagittally, the prostate can be viewed with two simultaneous planes (b). The 3D prostate image has been sliced in a coronal plane to view it in a plane not available using conventional 2D TRUS (c).

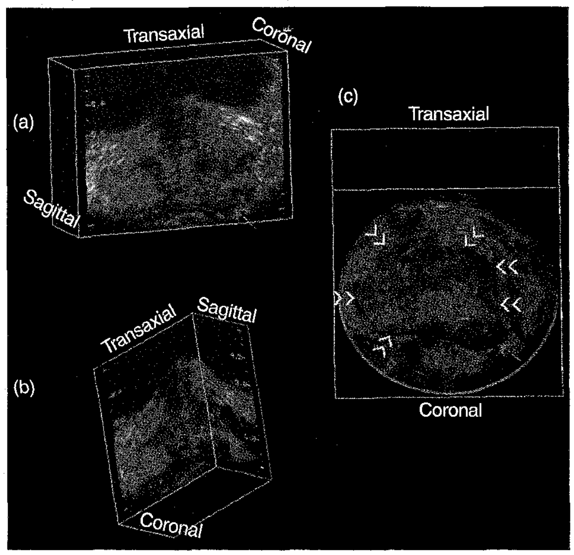

Fig. 3. The figure shows a 3D image of a prostate post-brachytherapy. The 3D image has been sliced in a sagittal plane to reveal a few brachytherapy seeds, which appear as white regions (a); and a coronal plane showing that the seeds are more evident in this plane (b). The coronal plane cannot be obtained with conventional 3D TRUS.

measured volume of the balloon. The results showed an rms error of 0.9% and an rms precision of 1.7%.

Volume Measurements of Prostates In Vitro

Six prostates, with seminal vesicles and some periprostatic fat attached, were harvested from fresh cadavers, fixed and stored in 10% formalin. After fixation, their volumes were measured by water displacement in a graduated cylinder, and found to range from 25 to 98 cm^3. A plastic container, lined with sponge to decrease sound reflection, was filled with a solution of 7% glycerol in distilled water. A wire grid was placed in the bottom of the container to support the prostates, which were angled at 25° to the vertical, mimicking the normal anatomical alignment of the prostate in the body relative to the position of the transrectal ultrasound transducer [6].

The 3D transducer assembly was fixed to a metal stand, with the distal end of the transducer immersed in the glycerol solution within 2 cm of the prostate. After allowing the solution to settle, a 3D image of each prostate was obtained, with an angle of rotation of about 100°. During this rotation, typically 100 2D ultrasound images were digitized and reconstructed into a 3D image.

The prostate volumes were measured by manual planimetry using a similar technique to the balloon volume measurements. Each prostate was "sliced" into 20 to 30 transaxial slices 2 to 5 mm apart, and the boundary of the prostate in each slice outlined. The volume was obtained by summing the area-thickness products of each slice [6]. A linear regression of measured vs. true volume yielded a slope of 1.006 ±0.007. The accuracy (rms deviation from the line of identity) of the measurements was 2.6%, and the precision (rms deviation from the best fit line) was 2.5%.

Use of 3D Ultrasound in Brachytherapy

In Vitro Seed Identification Study

It is now recognized that 3D ultrasound imaging has an important role to play in brachytherapy planning. Its role may be greatly expanded if brachytherapy seeds could be accurately detected and their locations determined. For this reason, we conducted a study to determine the variability of measuring the location of brachytherapy seeds in 3D TRUS images using a tissue-mimicking phantom. Twenty brachytherapy seeds were inserted into the phantom in a fan pattern, at varying depths. Three-dimensional ultrasound images of the phantom were then acquired using the 3D system attached to an Aloka SSD 2000 ultrasound machine, using the endo-cavity side firing probe.

Seven observers measured the Cartesian coordinates of all the seeds in the 3D image. Each observer "cut" into the 3D image to reveal sagittal sections of the prostate, and measured the x, y, and z coordinates of the seeds in that revealed view. This procedure was repeated twice for each observer. An analysis of variance (ANOVA) was performed to determine the standard error of measurement and the minimum detectable change in the coordinates. The results indicated that under ideal conditions, such as those found when imaging agar phantoms, the location of the seed can be determined at the 95% confidence level to better than 1 mm.

In Vivo Use of 3D Ultrasound in Brachytherapy

The results above demonstrate that brachytherapy seeds can be identified in 3D images of a phantom. Images of prostates *in vivo* show clutter, which may make identification of seeds more difficult. In order to assess the ability to distinguish brachytherapy seeds in patients using 3D ultrasound images, we performed a 3D scan on a patient who has undergone a brachytherapy procedure. Figure 3 shows three views of the prostate in which the 3D image has been cut in different planes to reveal the seeds. The 3D ultrasound images show that all the seeds are difficult to distinguish, and that improvements in the echogenicity must be achieved before all the seeds could be reliably identified.

Conclusion

Our 3D ultrasound imaging system for imaging the prostate can be interfaced to any conventional ultrasound machine, and can accommodate side-firing transrectal ultrasound transducers. After acquiring a series of 2D ultrasound images, a 3D image is reconstructed. The 3D image is available to the physician, allowing the prostate to be viewed interactively in multiple simultaneous planes, allowing better visualization of its internal architecture. This approach allows the physician to record and view the whole prostate in successive examinations, making 3D TRUS well-suited to performing prospective or follow-up studies. Our results indicate that 3D ultrasound imaging of the prostate has great potential as a tool for the diagnosis, therapy, and follow-up of prostate disease.

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Fuzzy Techniques

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