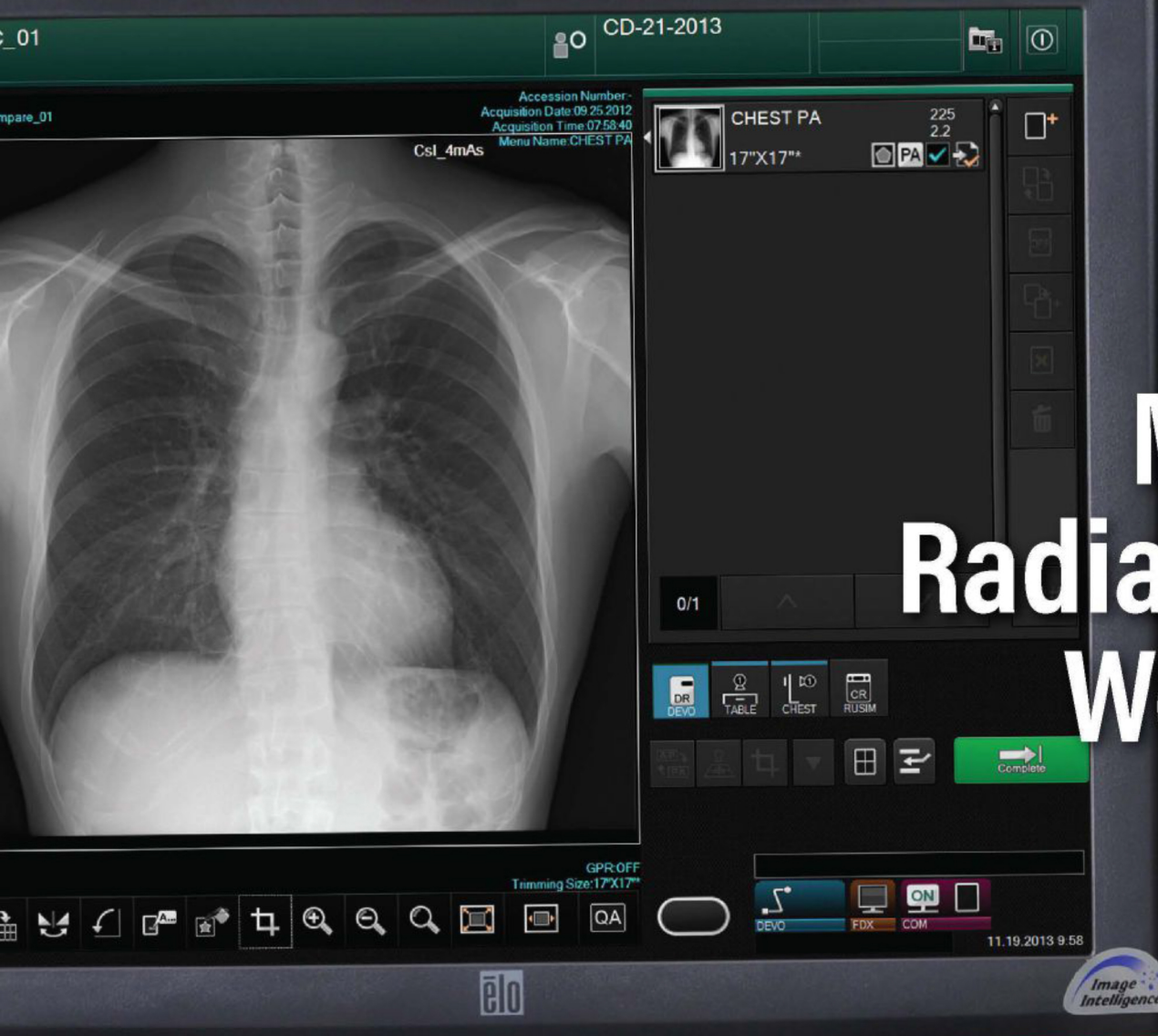


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Monitoring Radiation in the Workplace 3



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4-D Guided Prostate Treatment: **The Future of OIM-directed Therapies**

New information management technologies advance image guided treatment since tumor volume, capsular margins and aggression parameters are quantifiably evaluated before, during and after therapy in 3-D

By Robert Bard, M.D., DABR, FASLM

Extracapsular extension (ECE) is a major clinical indicator for brachytherapy or external beam treatment of prostate cancer. The prostatic capsule is a thin layer of compressed fibrous tissue and ultrasound imaging depicts the pericapsular fat as a strongly echogenic structure while magnetic resonance imaging (MRI) demonstrates a dark envelope. The capsule tends to be incomplete around the apex accounting for greater extraprostatic spread from apical tumors. Applying standard diagnostic criteria, capsular erosion must appear in two orthogonal views or in multiplanar 3-D volumetric sonography 2/3 planes. Unlike standard ultrasound where the operator moves the probe, volumetric 3-D transducers are stationary as 200-300 images are captured in 10 seconds, removing the problem of operator dependency and allowing rapid review and accurate comparison of pathology in subsequent studies. (See **Figure 1.**)

Capsular invasion occurs with infiltration of the cancer into the fibrous capsule. Capsular penetration is tumor invasion extending beyond the capsule that produces bulging, irregularity of the capsule and gross tumor noted invading the fascial planes, rectal serosa or levator sling muscles. Perineural invasion, a microscopic diagnosis, cannot be inferred from diagnostic imaging at this time. However, the nerve supply of the gland tends to follow the major arterial network and is imaged with color Doppler sonography (CDS) or power Doppler sono-angiography (PDS). Capsular lateral wall erosion is often best imaged in the coronal view on 3-D PDS, while posterior erosion usually is best depicted on the transverse 3-D PDS. MRI, with its inferior capsular resolution (including endorectal coil scans) may not always confirm extracapsular disease clearly exhibited on high-resolution sonography.¹⁻⁷ During examination of a suspicious capsule finding, the real time 4-D mode might be used to target the anomaly and better image the full anatomic extent of penetration with curvilinear probes.

Quantifiable Digital Scanning Versus Biopsy

The new optical dermatologic modalities of reflectance confocal microscopy (RCM) and optical coherence tomography (OCT) are highly accurate in detecting malignant capsular penetration and are used in other solid organ tumors such as breast, thyroid and prostate tumors with great accuracy, but limited depth penetration. Highly suspect areas are then checked for spread to the seminal vesicles, and a search is performed for lymphadenopathy to verify the disease is locoregionally confined and surgical intervention is unlikely at this time. Patients are reassured since they simultaneously see the 3-D picture as the real time exam proceeds in thoroughly logical, systematic staging. Four-dimensional sequencing (real time 3-D) permits image-guided biopsy of the most virulent area of the tumor and allows the pathologist to focus on strongly suspicious regions of the lymph node mass excised during prostatectomy. Similarly, during examination the patient may personally visualize extraprostatic

disease or seminal vesical invasion so plans for radiation or other therapies may be initiated in a timely manner.

Digital Imaging Reduces Complications

Fear of complications deters patients from seeking medical intervention so many opt for noninvasive diagnostic options. Cancer treatment effectiveness depends on the precise tumor volume and depth penetration measurements. However, many cancers provoke a benign local immune response or there may be co-existent inflammatory reaction that simulates a larger area of malignancy, such as cicatrix formation accompanying chronic prostatitis, that is indistinguishable on MRI from a stone or malignancy. Imaging highlights the true border of the tumor, optimizing targeting for healthy tissue sparing and resulting in a narrower treatment zone and lesser side effects.

Doppler Applications

Blood vessel mapping using the various Doppler modalities is routinely used in both cancer treatment and reconstructive preoperative planning. In cancer radiation, the presence of aberrant large veins or significant arteries in the treatment field may allow post-treatment vasculitis to be minimized. Advanced 3-D Doppler systems allow for histogram vessel density measurement of neoplastic angiogenesis. (See **Figure 2.**) This baseline of neovascularity is used worldwide as a reliable treatment parameter and serves as an accurate surrogate endpoint.⁸⁻²²

Low grade prostate cancer identified by 4-D volumetrics clearly delimited by the capsule and of low tumor vessel density is followed serially in 6-month intervals. Subsequent capsular invasion or increase in vessel density by histogram analysis requires urologic or oncologic measures. Primary bladder cancer or extracapsular extension into the bladder is evaluated concomitantly with the prostate and neovascularity and wall invasion noted before surgical referral. Rectal and bladder post-radiation effects may be moderated by pretreatment placement of tissue buffering devices under ultrasound image guidance.

Contrast Enhanced Ultrasound (CEUS)

In 1990 Rodolfo Campani, M.D., director of the University of Pavia Radiology Department, developed ultrasound contrast-enhanced cancer imaging for liver tumors followed by David Cosgrove, M.D. (London), Nathalie Lassau, M.D. (Paris) and Carlo Catalano, M.D. (Naples), for breast, prostate and melanoma respectively. CEUS is currently used worldwide, but not fully FDA-approved in the United States. Microbubble media show tumor neovascularity with exquisite detail, evaluating therapeutic response in solid organs. This distinction is important since the international response assessment in solid tumors (RECIST) studies demonstrated tumor enlargement during treatment may be related to apoptotic cell death with cystic degeneration or immune cell infiltration destroying malignant tissue while

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increasing the visualized tumor volume. Doppler ultrasound or CEUS reliably verifies decreased malignant angiogenesis in these cases instead of using biopsy, contrast computed tomography (CT) or DCE-MRI for confirmation. Thermal treatments such as cryotherapy, high-intensity focused ultrasound (HIFU) or laser ablation are designated complete when penetrating cancer arteries are no longer detectable. It must be noted that prostatitis and post-treatment changes by radiation or other therapies distorts the expected imaging anatomy by most modalities, and the true evaluation of recurrence is best determined by functional vascular perfusion studies that are superior surrogate tumor markers to other clinical indicators. A recently recognized

therapy. Shrinking tumors may likewise be biologically viable as is occasionally seen from the aggressive desmoplastic reaction to certain high-grade breast cancers. Post radiotherapy imaging in successful cases may show decrease in tumor neovascularity in as short a time period as 1-2 weeks, suggesting short interval neovascular evaluation as a better indicator of effective response than standard protocols. In the future, ionizing treatments may be considered effective when tumor vessel perfusion has completely ceased at a 3-month scan interval and further biopsies possibly obviated. Post-radiation prostate-specific antigen (PSA) spikes are quickly shown to be false positives due to prostatitis

immuno-oncologic response limiting positron emission tomography (PET)/CT accuracy is termed "pseudo-progression" demonstrating overall tumor burden increases during successful

or bone metastases rather than actual recurrence in the treatment glandular area.

Margin Delineation

Advances in laser/optical devices allow near microscopic tissue analysis of the cells by noninvasive testing. Real time microscopy during surgery verifies the tumor border is clear in cases of skin cancer, and future use in breast and prostate cancer treatment is under clinical study. In true capsular penetration, radiation treatment becomes a prime clinical option. Since the 18 MHz probe is directly in contact with the capsule, the resolution is five times greater than MRI capability. DCE-MRI is routinely used to verify malignant lymphadenopathy or bone metastases, and has been highly successful after 3-D/4-D imaging has ascertained and localized the extraprostatic disease.²³ Another potential use of margin neovascularity is the problem with anatomic pathologists seeing biopsy specimens that appear malignant but not being able to assess if the microscopically abnormal cells are biologically active. Some of the newer optical applications image capillary blood flows, meaning the total absence of microcirculation may signify a treated tumor under

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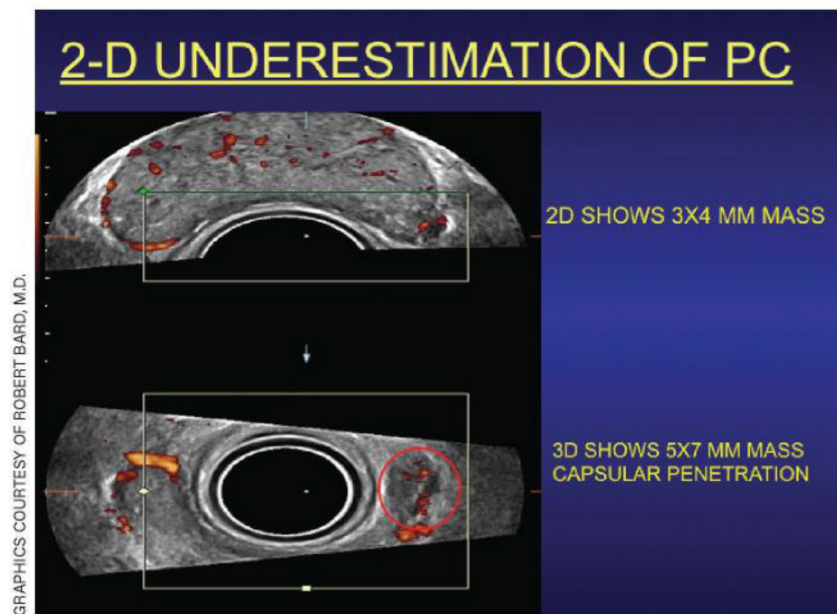


Figure 1. 2-D (top) vs 3-D (bottom). The irregularly margined left tumor mass that bulges the lateral capsule appears three times the volume on the multiplanar 3-D/4-D image reconstruction and shows complete extraprostatic extension. *Note:* This anterolateral lesion is not clinically palpable.

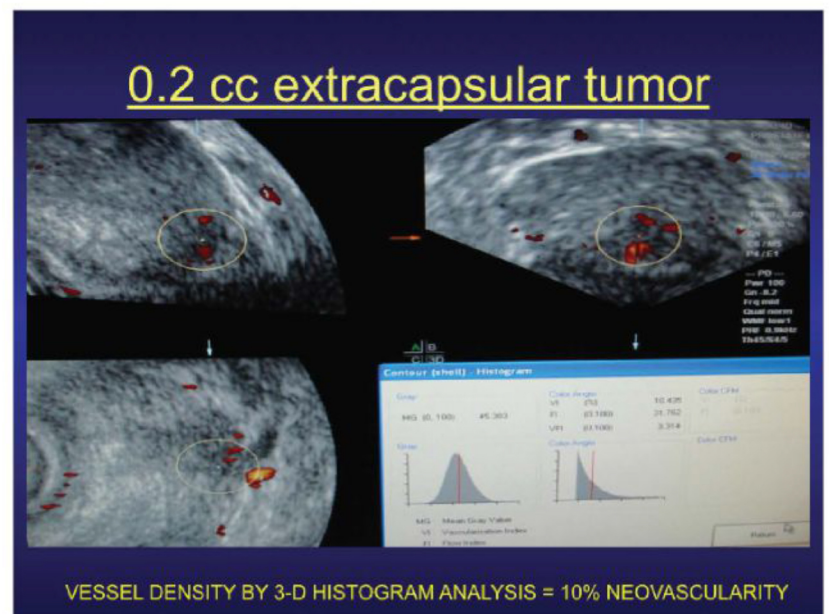


Figure 2. Histogram-volumetric study shows extracapsular tumor has a 10 percent malignant vessel density, which can be used as a reference measurement to assess treatment effect on serial scans.

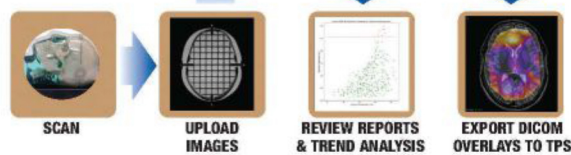
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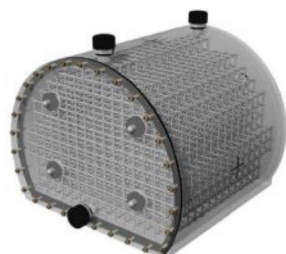
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