Chapter 4
Image Guidance Systems for Brachytherapy

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Introduction

- Image guidance is inextricably linked to the evolution of brachytherapy. This chapter will present an overview of the image guidance methods relevant for brachytherapy today or beginning to gain acceptance
- There are many perspectives one can have on imaging:
  - Applicator visualization vs. anatomy delineation vs. functional information
  - Single modality vs. multiple modalities
  - Contrast vs. depth vs. resolution vs. spatial accuracy
  - 2D vs. 3D vs. multidimensional
  - Ionizing vs. nonionizing radiation

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- With the advent of multiple imaging modalities, medical image registration has emerged as an active research field
- In brachytherapy, multiple applications are typically associated with multiple image datasets, each containing anatomy, applicators, and dose distributions in 3D, thus posing the difficult problem of adding dose to distorted targets and OARs for the purpose of evaluating plans
- Deformable registration and dose accumulations are not only difficult and interesting problems today but fields of research on their own
- The final goals of image guidance in brachytherapy are:
  - To reduce invasiveness by allowing minimally invasive procedures
  - Increase accuracy
  - Shorten procedure times and
  - Ultimately improve outcomes
- Without the claim for completeness and with the constraint of space, we hope that this chapter will give the reader a good overview of where image guidance is today in brachytherapy and where it might go tomorrow

2D

Planar Radiography

- Provides a 2D representation of the patient anatomy in a given orientation
- Has high resolution but low soft tissue contrast
  - Overlay of the anatomy makes it difficult to clearly distinguish individual soft tissue structures
  - Bones and areas of higher atomic number (i.e., metals, contrast-filled catheters/balloons) can be more easily differentiated

- Readily available but provides limited information which can impact treatment quality
- Used in brachytherapy as a tool for source localization in implants, treatment planning, and applicator insertion evaluation
- At least two images are necessary to obtain 3D information
- During source localization, the position and orientation of the sources is determined relative to the patient anatomy
  - Orthogonal images (images taken with a 90° separation) commonly used
    - It can prove difficult to relate the source on one orthogonal image to the other due to different appearance of anatomy in the two views
    - Poor image quality on the lateral film due to patient thickness in sites like the pelvis also increases the difficulty of associating sources on the two films
  - Non-orthogonal image pairs (isocentric images at angles <90°) can also be used
    - Advantage: Views are more similar (source position during image acquisition is closer between the two films)—Facilitates source identification
    - Disadvantage: The smaller the angle difference in the two images, the less accurate the 3D spatial localization becomes
  - Other 2D technique for source localization: "Stereo" films
    - Acquisition of two patient images with a linear displacement between the two
    - Done by moving either the patient or the X-ray source
    - Provides an easier mean of source localization in comparison to orthogonal film—the anatomy between the two films is easy to correspond
    - Has the worst depth reconstruction accuracy of the three [1]

- Source localization used in the past to calculate post-implant dosimetry of permanent implants
  - Since source positions cannot be accurately known within the patient anatomy, this technique is used to calculate the matched peripheral doses (contour volume dose equals the dose of the target) [1]
    - For prostate implants, this parameter is a poor indicator of the actual dose delivered to the gland [2]
  - Technique no longer routinely used in the clinic as Transrectal Ultrasound (TRUS) imaging is considered the standard for permanent prostate brachytherapy treatment planning [3]
- Treatment planning with radiographs:
  - Difficult to relate the dose distribution delivered to the dose received by the target and organs at risk
    - Target volume to be treated usually not visible due to lack of soft tissue contrast
    - Lack of true volumetric information
  - Limited visibility of soft tissue—plan based on dose prescription points and organs-at-risk points for dose specification
  - Example: Use of point A in the treatment of locally advanced cervical carcinoma using Tandem and Ovoid/Tandem and Ring applicators
    - Point A: Dose prescription point—Represents the crossing of the ureters with the uterine artery
    - Soft tissue is not visible on radiographs, a variety of surrogates used to localize this point on films = inconsistencies in the dose specifications due to lack of robustness of some of the surrogates
    - American Brachytherapy Society guidelines published in 2012 indicate that the point should be placed by tracing a line between the center of the ovoids (or most-lateral dwell positions in the ring), identifying the point at which it crosses the tandem, and moving superiorly along the tandem a length of 2 cm + the radius of the ovoids (or superior thickness of ring cap), as seen on the

lateral film. Then, the points should be placed laterally, 2 cm on each side, perpendicular to the tandem as seen on the AP film [4]
    - Use of two orthogonal films is required
    - Assumes a high quality applicator insertion—any deviation of the applicator geometry from the ideal (tandem and ovoids bisect on the AP film, ovoids are not displaced inferiorly to the flange, and they overlap each other on the lateral film) will affect the placement of the prescription point
    - If films show poor applicator geometry, placement should be corrected before proceeding [4]
    - Improper applicator geometry is detrimental to treatment outcomes
- Orthogonal radiographs are a good tool to evaluate brachytherapy applicator insertion quality (for tandem and ovoids/tandem and ring), even when volumetric treatment planning techniques are used [5, 6]

Fluoroscopy

- Continuous planar radiography to observe the patient's anatomy in real time
- Can be used during interstitial and permanent seed implants to monitor seed and needle positions
- This modality is complementary to ultrasound (US) during implants—sources cannot be easily seen on US but are readily seen in fluoroscopy [7]
- Registration of source positions from fluoroscopy on US images is being considered as means of real-time treatment planning for permanent prostate implants [7]

Ultrasound

- Uses sound waves to image the anatomy
- Nonionizing, inexpensive, and allows visualization of the anatomy in real time

- Quality of the image is highly dependent on the operator.
- Images can be difficult to interpret [8]
- Highly useful to guide applicator and needle insertions [2–4, 8, 9]
- During tandem insertion for gynecological procedures, the use of a transabdominal or transrectal probe as the tandem is placed helps reduce rate of uterine perforation [4]
  - Treatment with a tandem that has perforated the uterus can lead to significant irradiation and toxicity of adjacent organs at risk such as the bowel or bladder
- To maximize visualization of the pelvic anatomy when using US, there should be approximately 200 cm^3 of saline in the bladder [4]
- Work has been done to show the potential use of 2D US to plan brachytherapy treatments for gynecological cancers [10]
  - Images provide better soft tissue contrast than radiographs
  - Allows for more accurate visualization of organ boundaries and target volumes which can serve to create a more conformal plan even without a full 3D volumetric dataset [8, 10]
  - Figure 4.1a–d shows the ease of visualization of the soft tissue anatomy and applicator with newer US technology and it compares it to a sagittal MRI view
- US guidance during interstitial implants can help determine depth of insertion and avoid placement of sources outside the target volume = Reduced risk of bladder and bowel perforation, and better target implantation [4, 9]
- Transrectal US (TRUS) imaging commonly used for needle insertion guidance during transperineal prostate implants—recommended approach by ABS and GEC/ESTRO [3, 11]

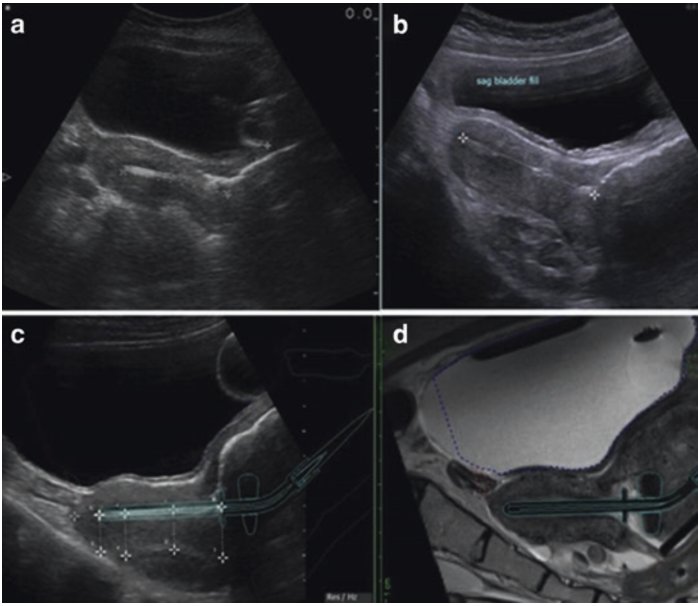

FIG. 4.1. Example of improvements in quality of ultrasound images with new ultrasound technology. (**a**) Sagittal view of applicator in uterus taken in 2008 with Falcon ultrasound unit (BK-Medical, Herlev, Denmark). (**b**) Sagittal view of applicator in uterus taken in 2010 with Flex focus 400 ultrasound unit (BK-Medical, Herlev, Denmark). (**c**) Sagittal view of applicator in uterus taken in 2012 with Flex focus 400 ultrasound unit (BK-Medical, Herlev, Denmark). (**d**) Sagittal view of applicator in uterus on MRI taken in 2012 same patient as in (**c**) (Used with permission of the Peter MacCallum Cancer Center and Elsevier from van Dyk S et al. Ultrasound use in gynecologic brachytherapy: Time to focus the beam. Brachytherapy. 2015 May–Jun;14(3):390–400)

3D

- Use of volumetric imaging for treatment planning of brachytherapy procedures has improved treatment outcomes and reduced toxicities
- 3D anatomical information during treatment planning allows for
  - Better target volume definition and organ at risk visualization
  - Improved dose optimization
- Several 3D imaging modalities are available for use—strengths and weaknesses vary and their validity for brachytherapy use depends on the anatomical site of interest

Computed Tomography (CT)

- Provides cross-sectional images of the anatomy = better soft-tissue definition than planar imaging
- Physicians can delineate the tumor volumes and organs at risk to allow for dose optimization of the treatment plan
- Better soft tissue contrast than planar imaging, but still inferior to Magnetic Resonance Imaging (MRI)
- Use is a lot more prevalent than MR because it is not as resource intensive and a large portion of departments have a CT scanner on site [8, 12]
- Excellent choice for source localization (within the limits of slice thickness and partial volume effects of the scanner), and it is preferred over radiographs [1]
  - Uncertainty of proper source identification no longer a concern, sources can be easily distinguished from the surrounding soft tissue
  - Dose distribution calculated from the sources can be directly evaluated with respect to the patient's anatomy depicted on the CT scan

- When utilizing CT for interstitial treatment planning, the choice of needles is essential to the image quality
- Titanium or flexible plastic needles produce fewer artifacts than stainless steel needles = better volume definition [4, 9]
- CT imaging is not the optimal imaging modality for prostate delineation
  - Gland not clearly visible
    - Posterior portion of prostate and anterior wall of rectum cannot be easily differentiated in non-contrast CT
    - Apex of prostate blends with anterior portion of the levator ani muscles and adjacent neurovascular bundles are not distinguishable—often get contoured as prostate [2]
  - Subjective delineation, yields inter/intraobserver variability = overestimation of the prostate volume in comparison to US or MR [7, 13]
  - Dosimetric parameters calculated from post-implant CT contours yield inter- and intraobserver variability in dose reporting [2, 7]
  - Despite these issues, CT often used for post-implant dosimetry due to ease of availability at most centers and clear visibility of the implanted sources
  - Contouring issues are well known, physicians can try to minimize them as they draw the volumes. Figure 4.2 illustrates differences in prostate shape and size when contoured with 3D TRUS, MR, and CT [13]
- CT can also be used to evaluate the potential pubic arch interference in prostate implants
  - Largest axial dimensions of prostate can be projected onto slice displaying the pubic arch to check for potential issues [2]
  - Important: If CT scan is not performed in the same position as needle insertion, differences in expected versus actual clearance may arise

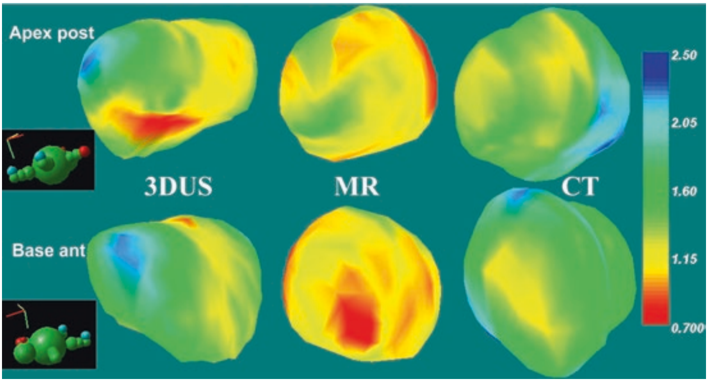

FIG. 4.2. Standard deviation (in mm, see color bar at right) in radial distance to contour vertices for 14 observations, averaged for all patients. The difference in apparent size reflects the differences between modalities. *CT* computed tomography, *MR* magnetic resonance, *3DUS* three-dimensional ultrasound (Used with permission from Smith WL et al. Prostate volume contouring: A 3D analysis of segmentation using 3DTRUS, CT, and MR. Int J Radiat Oncol Biol Phys. 2007 Mar 15;67(4):1238–47)

- CT scans are used for treatment planning of HDR prostate treatments after TRUS-guided needle insertions
  - Due to the time elapsed between planning and treatment delivery, caudal needle retraction has been observed and should be corrected and verified [14]
- Cone Beam CT (CBCT) imaging can be utilized to check needle positions
  - Study by Holly et al. showed a mean internal displacement of catheters of 11 mm during pre-treatment CBCT, which was corrected before dose delivery [14]
  - Alternative workflows are being investigated to alleviate treatment uncertainties stemming from prolonged time between insertion and delivery [15, 16]

  - Use of TRUS for treatment planning is being considered, but needle reconstruction on TRUS is challenging and too inaccurate
  - Combination of TRUS for soft tissue delineation and CBCT for needle reconstruction can lead to acceptable real-time dosimetry [16, 17]
  - CBCT has also been used as an alternative to orthogonal film planning for gynecological diseases [18]
- Use of CT images for gynecologic treatment plans more common than MR despite its soft tissue contrast inferiority [12]
  - Due to the difficulties in assessing the target volume in CT, CT contouring guidelines specific to treatment planning of cervical brachytherapy are available [19]
  - Use of applicators that do not cause severe image artifacts is important and should be considered to maximize image quality

Ultrasound

- Transrectal Ultrasound (TRUS): Standard treatment planning modality for permanent perianal prostate seed implants [3], technique first used in 1983 by Holm et al. [20]
- Prostate clearly visible in the images and patient position between pre-implant scan and insertion can be closely replicated—TRUS used to guide needle insertion in the operating room
- When using TRUS, patient is positioned in the lithotomy position and a transrectal probe is used
  - Probe attached to stepping device that stabilizes it and allows for precise superior-inferior movement in set intervals. Figure 4.3 shows an illustration of the apparatus [21]

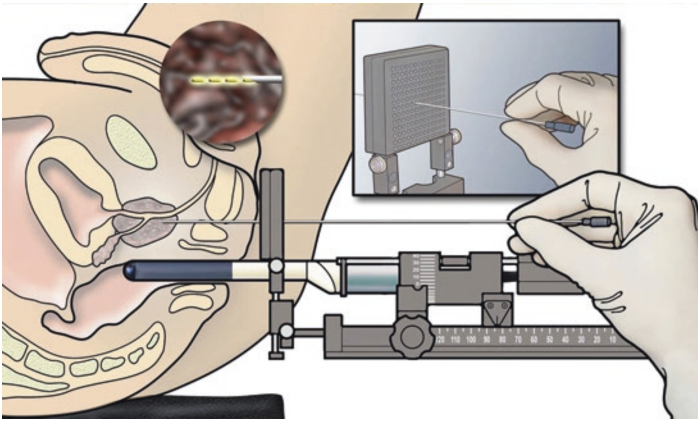

FIG. 4.3. Illustration depicting the needle insertion and seed implantation during a permanent prostate implant procedure with transrectal ultrasound guidance (Used with permission of Analogic Corporation from “Transrectal ultrasound guided prostate brachytherapy,” by Brendan Carey MD, ebook)

- TRUS pre-implant volume study for treatment planning:
  - Axial slices of prostate, 5 mm apart, coverage at least from base to apex [2]
  - Overlay of insertion template placed on images to facilitate treatment planning
  - Patient should be in same position for pre-implant planning US scan and needle insertion
- Pre-implant planning with TRUS is preferred although MR can also be used [3]
- CT alone is not recommended over TRUS or MR because it is less reproducible, and the prostate volume is better identified using TRUS [7]
- Urethra visible on US—planner can avoid seed placement in or near it to limit its dose and minimize treatment-related complications
  - Aerated gel can be inserted into urethra to increase contrast and facilitate visualization [2]

- TRUS equipment with the capability of displaying both axial and sagittal slices:
  - Aids in proper seed placement in superior capsule of prostate
  - Helps visualize gland movement during needle insertion
- TRUS can also be used to check pubic arch interference during pre-implant scan [2]
  - Hard to identify the pubic arch on TRUS, but bone-soft tissue interface can be visualized and marked on the US screen
  - Probe can then be moved to visualize prostate on consecutive axial slices to check for clearance
- US inadequate for post-implant dosimetry: Prostate can be clearly visualized but the seeds cannot [7]
  - Image registration between TRUS and CT could alleviate this issue, but tissue distortion due to the probe in the rectum makes it a challenging problem. Effects of TRUS probe on prostate shape are visible in Fig. 4.2 [13]
- 3D US currently not used in planning of gynecological malignancies, but there is interest because it is a more readily available technology in developing countries [8]
- Use of robotic systems for image-guided brachytherapy is under development—Most currently geared towards prostate implants
  - Compilation of available systems through January 2012 has been published by AAPM in conjunction with GEC-ESTRO [22]
  - Systems use either TRUS or MR for image guidance and some even allow for automatic needle insertion and seed delivery without a physical template
- Doppler ultrasound imaging identifies areas with measurable blood flow signal
  - Can identify foci of growing tumor in the prostate by imaging increased microvessel density areas [23]—identification of intraprostatic lesions could be applied to tailor dose distribution to specific disease location

  - Other applications of Doppler in brachytherapy include the detection of major vessels during interstitial implants to avoid injury [24]

MRI

- MRI is a noninvasive imaging technique that provides:
  - Volumetric information on the density of the certain atomic nuclei
  - Information on the structure, dynamics, and chemical environment of molecules
- Nuclear magnetic resonance (NMR), first observed in 1945, relies on the interaction of nuclei of certain magnetic isotopes with a static magnetic field
  - While nearly every element has at least one NMR active isotope, the common NMR active nuclei are H-1, C-13, P-31, and N-15
  - The easiest to observe nuclei have spin $I = 1/2$ and very high (≈100 %) abundance. Hydrogen (H-1) is particularly interesting because of the abundance of water in the human body, a low precession frequency at a 2 T field (~90 MHz), and relaxation times that make fast acquisitions of many FID (free induction decay) signals possible in times of the order of minutes
  - While NMR on heavier elements like P-31 or Na-23 (naturally abundant in the body) can reveal very interesting information (e.g., energy metabolism in various disease sites), multinuclear imaging is currently only a research tool
- MR spectroscopy (MRS) allows measurements of tissue metabolites levels. For example, in prostate the metabolites commonly measured and correlated with Gleason score are choline, spermine, and creatine
- In MRI, besides the density of protons, contrast can be obtained to demonstrate different anatomical structures or pathologies

  - The return to equilibrium state of the nuclear spins after excitation is governed by the independent processes of T1 (spin-lattice) and T2 (spin-spin) relaxation. T1 and T2 are tissue specific
  - T1 is useful for identifying fatty tissue and in general for obtaining morphological information of soft tissues
  - T2 image weighting is useful for detecting edema and inflammation and assessing zonal anatomy for sites like prostate, cervix, and uterus
- While imaging anatomical structures or blood flow (typically associated with functional MRI) does not require contrast agents, such agents (gadolinium is a very common one) are sometimes used intravenously before or during the MRI to increase the speed at which protons are realigning with the magnetic field.
  - The shorter the relaxation time, the brighter the image
- Another parameter that can provide very interesting information is diffusion
  - Unlike in an isotropic medium, where water molecules are moving randomly, in biological tissues water motion is constrained by the morphology of the tissue
- Diffusion weighted imaging (DWI), for example, can image swelling due to changing (increase) of barriers to water diffusion. While most MRI imaging protocols take minutes or longer, a real-time MRI is possible due to new imaging pulse-sequences (FLASH) and fast iterative image reconstruction, leading to speeds of 50 frames per second at a resolution of 1–2 mm
- Being a nonionizing radiation imaging method, MRI has the advantage that can be done as many times as necessary
- From the general perspective of radiotherapy, MRI has two major limitations:
  - Spatial image distortions
  - Missing electron density information

- For brachytherapy, both these limitations are mild, since a small field will likely have smaller distortions and for HDR energy, the water world of TG-43 is a reasonable approximation at least for pelvic treatment sites (cervix, prostate). In the newer paradigm for dose computation, the Model Based Dose Computation Algorithms (MBDCA), electron density, and other material properties (interaction cross sections, tissue mass density, atomic number distribution) need to be assigned on a voxel-by-voxel basis. A CT to MRI co-registration, normally sufficient for EBRT dose computation, is needed but not sufficient for brachytherapy if dose is to be computed using MBDCA
- Field strength of the MRI scanner is important:
  - Lower fields (0.2–0.5 T) allow for larger bores or open magnets reducing patient claustrophobia. The price to pay is poor image quality
  - In order to increase quality and resolution, one has to consider fields in the range 1.5–3 T, but here the price is an increased image distortion
- MR compatibility:
  - Applicators used in brachytherapy, when MRI is used for imaging, have to be MR compatible. If MRI is used in an interventional mode, so have to be all the instruments, probes, needles, etc
  - When dummy markers are needed to outline the path of the radioactive source within applicators, catheters filled with $CuSO_4$ solution can be used to insure visibility on MR images
- While MRI for permanent seed implants evaluation is not as common as the CT-based one, it is a safe procedure at fields less than 3 T. Eddy currents induced in the titanium shells produce very little heating and artifacts during routine imaging. Detecting seeds in MR images is nontrivial as they look like voids, and they can compete with needle tracks (also voids). While MRI presents a clear advantage for delineating anatomy, when it comes to identifying seeds, a reason-

able solution is fusing MRI and CT and retrieving the seed positions from the CT dataset

- MRI, MRS, and mpMR (multi-parametric MR, a combination of T2, ADC, DWI, DCE, and proton magnetic resonance spectroscopy imaging) are beginning to be commonly used for detecting and staging prostate cancer [25], as well as planning the biopsy and the treatment plans for both LDR and HDR
- Whether in the setting of initial treatment or salvage after a recurrence, MR images of various flavors are typically co-registered with US (Ultrasound) or CT, which are primary imaging and real-time guidance methods (US) for these types of treatments. MRI allows for delineating of foci of disease and usually an MR-based or -augmented plan involves boosting these foci at higher doses
- In 2005, the Groupe Europeen de Curietherapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) published recommendations on contouring of tumor target and organs at risk and reporting of dose volume parameters for image-guided brachytherapy (IGBT) for locally advanced cervix cancer [26], thus creating an impetus towards increased use of MRI
- For cervical cancer, the obvious benefit of improved tumor detection and delineation is somehow diminished by the difficulty of integrating MRI into a HDR intracavitary brachytherapy workflow
- A number of scenarios can be envisioned in order to take advantage of information contained in MRI images, but the main difficulty to overcome is the registration on MRI depicted anatomy without applicators to the CT anatomy with applicators, given the significant changes in anatomy produced by applicators. One elegant way to solve this problem is to place a Smit sleeve during the first CT-planned fraction, acquire an MRI scan with no applicator in place, and then co-register subsequent CT datasets to the MRI scan using the Smit sleeve visible in both CT and MRI [27]

PET

- Positron Emission Tomography is a nuclear medicine imaging method producing a 3D image of functional processes in a body
- A short-lived positron emitting radionuclide (F-18, O-15, N-13, Ga-68) is transported to the site to be imaged by an organic molecule (radiotracer), usually injected in the blood stream. After a wait period (~1 h), needed to increase concentration in the tissue of interest, the acquisition process starts
- The radioisotope decays through positron emission, and the positron emitted travels a short distance until it is annihilated by interaction with an electron. In the process, a pair of opposite photons is produced and it is this pair, detected in coincidence, which locates the site of the initial decay
- The most used radiotracer is fluorine-18 (F-18) fluorodeoxyglucose (FDG), thus making FDG-PET almost synonym with PET. Since FDG is an analog of glucose (a sugar), high uptake areas will indicate high metabolic activity and glycolysis of cancer cells and depict metabolic abnormalities before morphological alterations occur
- 18F-FDG PET/CT has been primarily used as a diagnosis, staging, and restaging tool essential for an optimal management of cancer patients
- It has also been used to distinguish responders from nonresponders before any reduction in tumor size occurs. 18F-FDG PET/CT acquires PET and CT data in the same imaging session and allows accurate anatomical localization of the lesions detected on the 18F-FDG PET scan
- The combined acquisition of PET and CT has synergistic advantages over its isolated constituents and minimizes their limitations while enhancing each technique's advantages

- In the management of cervical cancer, lymph node metastasis is one of the poor prognostic factors, and PET-CT is more sensitive than other techniques (CT, MRI) for detecting pelvic and para-aortic lymph node metastasis [28]
- Thus, PET, by virtue of its lymph node detection, can upstage the clinical stage, modify treatment decision-making, and allow the radiation oncologist to extend the radiotherapy volume for inclusion of the metastatic lymph nodes. In brachytherapy, success is predicated on our ability to accurately define a high risk clinical target volume (HR-CTV) [26]
- FDG-PET/CT not only has the advantage that allows a good delineation of the tumor, but unlike MRI, does not require special applicators. Evaluating the utility of sequential 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) imaging for brachytherapy treatment planning in patients with carcinoma of the cervix, the investigators found that 9 of 11 patients had decreasing tumor volume, and 3 patients had complete remission before treatment was completed [29]
- In prostate cancer, there is no established role for 18F-FDG PET/CT in the assessment of disease, since it has a low accuracy owing to the relatively low metabolic rate of the tumor as well as the interfering adjacent urinary excretion of the tracer. However, other new PET radiotracers such as 11C-choline and 18F-fluorocholine have shown promising results in the management of prostate cancer. In a recent study [30], it was shown that combining MRI and 18F-fluorocholine (FCH) PET/CT for patients with a biochemical relapse (BR) after prostate radiotherapy or brachytherapy, the site of relapse was identified in about 70 % of patients, thus facilitating the selection of the patients for local salvage treatment. A high detection rate by 11C-choline PET/CT of extracapsular disease might become a clinically useful tool in management of prostate cancer patients

- Breast is another disease site in which 18F-FDG-PET/MR is used for preoperative cancer staging, with MRI having a higher sensitivity for primary tumors and PET for nodal metastases. In restaging, a major advantage of FDG PET imaging compared with conventional imaging is that it screens the entire patient for local recurrence, lymph node metastases, and distant metastases during a single whole-body examination using a single injection of activity, with a reported average sensitivity and specificity of 96 % and 77 %, respectively [31]

Challenges in the 2D to 3D Transition (Going from Points to 3D Geometry to Functional Structures)

- Traditionally, brachytherapy treatment planning performed using 2D films, with dose prescription and calculations to reference points
  - Poor soft tissue visualization in planar films—treatment plans could not be adapted to patient-specific anatomy
  - Organ dose reference points (defined by the International Commission on Radiation Units (ICRU) report 38 [32]) used to estimate the maximum dose received to these tissues. Figure 4.4a–c shows images from orthogonal films, CT and MR
- Use of 3D imaging much more time consuming and resource intensive, especially when using MRI, but superior visualization of anatomical structures yields more patient-specific, higher quality treatment plans
- For some brachytherapy procedures, such as prostate implants (TRUS with stepping devices), 3D imaging is commonplace and volumetric treatment planning is widely practiced
- More hesitation for gynecological treatments—doubts about necessity/value of 3D imaging for planning since

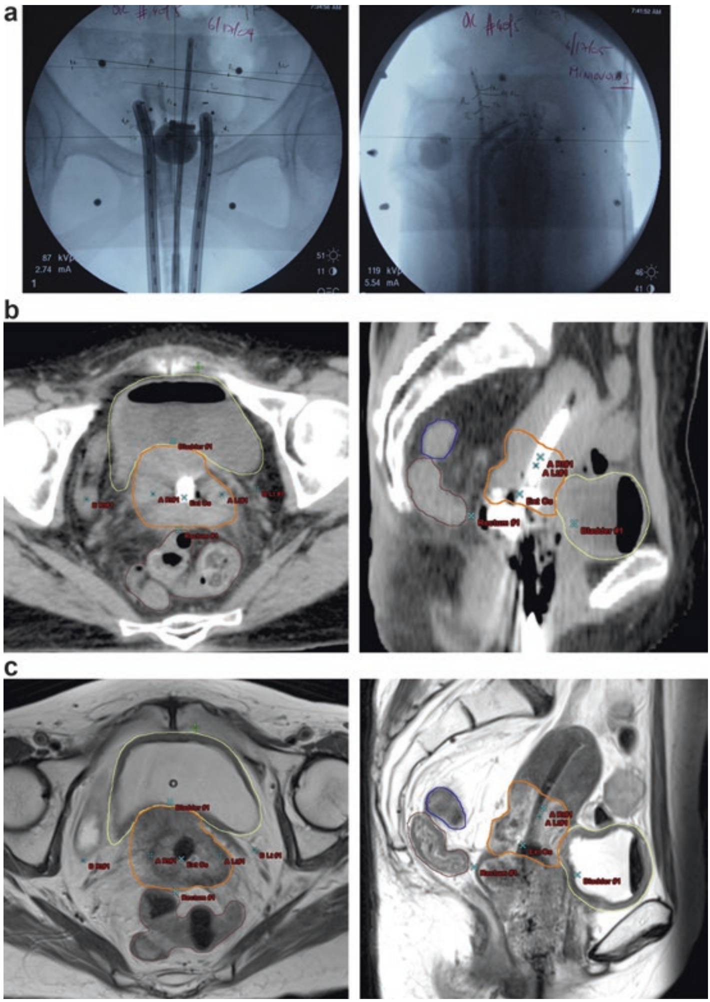

FIG. 4.4. (**a**) AP and lateral radiographs showing point A, point B, bladder and rectal and vaginal surface points. (**b**) CT images with point A, point B, HR-CTV (*orange*), bladder (*yellow*), rectum (*brown*), and sigmoid colon (*blue*). (**c**) MRI images with HR-CTV, bladder, rectum, and sigmoid colon. *CT* computed tomography, *HR-CTV* high-risk clinical target volume, *MRI* magnetic resonance imaging (Used with permission from Harkenrider MM et al. Image-Based Brachytherapy for the Treatment of Cervical Cancer. Int J Radiat Oncol Biol Phys. 2015 Jul 15;92(4):921–34)

historical 2D outcomes for cervical cancer management are good

- 2D planning achieved good tumor control and infrequent major complications were seen for treatments of cervical cancer, but visualization of 3D anatomy, using either CT or MR, has significantly improved the tumor control probability and minimized the normal tissue toxicity [33–35]
- Point A defined based on applicator, not tumor
  - Always a fixed distance away from applicator-does not account for the actual target volume to be treated
  - Might lead to a prescription lower than necessary for bulky disease or higher for small target volumes [36]
  - 2D planning based on point doses = oversimplification of the dose distribution of brachytherapy treatments and its effects on the anatomy of interest
  - Volumetric dose parameters used to evaluate 3D treatment plans include the D90 %, D100 %, and V100 % for the target volume (along with the V150 % and V200 % for interstitial plans)
- Several publications highlight the discrepancies between ICRU 38 organ point doses and volumetric dose parameters calculated based on 3D planning, especially for the bladder [5, 33, 34, 37–39]
  - Volumetric parameters used to evaluate organs at risk (OARs): D2cc, D0.1cc [4]
  - The ICRU reference bladder point has been reported to underestimate the D2cc by as much as 3.5 times [5]
  - The rectal reference point has shown better correlation with the D2cc of the rectum, studies in the literature have reported the ICRU rectal reference dose point results in doses that are 1–2.5 times lower than the maximal dose received by the rectum [5, 37]

    - Underestimates of the actual dose delivered to the OARs are likely the reason why higher rate of toxicity is seen in patients treated with 2D versus 3D planning [5, 33]
- 3D imaging found to be a cost-effective option over traditionally 2D treatment plans for sites such as cervical cancer [40]
  - Use of CT imaging for cervical cancer implants has been reported to be about 55 % in the United States [4]
  - Inspection of the implant with 3D scans also allows identification of applicator or needles that have perforated organs and should be repositioned, or not loaded during treatment = minimizes toxicity [4, 9]
- Use of 3D image-based planning has improved the outcomes of many brachytherapy procedures from permanent prostate seed implants to intracavitary treatments for gynecological diseases
- Better and more consistent definition of treatment volumes and dose prescriptions yield better plans and better dose reporting for treatment outcome evaluations

Other Imaging Methods Specific to Brachytherapy

- Anatomy is delineated in various imaging modalities and while model-based methods have been around for a while, it still requires a significant effort from physicians. Similarly, despite recent supervised detection algorithms and library of solid applicators, a planner will spend considerable time outlining applicators in the body
- An elegant solution, which requires a different type of imaging, involves the use of a tracking device. Tracking devices, despite not being common in brachytherapy, are an essential component of image-guided surgery systems

- Since optical trackers are difficult to use in a crowded clinical environment because of their unobstructed markers-to-cameras line-of-sight stringent requirement, electromagnetic trackers were developed and they are relatively new for clinical applications
- These systems localize small electromagnetic field sensors in an electromagnetic field of known geometry
  - Their main advantage is that they have no line-of-sight limitation, but their disadvantages include susceptibility to distortion from nearby metal sources and limited accuracy compared to optical tracking
- A number of research groups have developed solutions for automatic catheter reconstruction using electromagnetic tracking in brachytherapy environments.
  - The EM-tracked catheter representations were found to have an accuracy of <1 mm when compared with TRUS- and CT-user-delineated catheters, in the laboratory environment as in the brachytherapy operating room [41]. Reconstruction times are of the order of seconds, thus making automatic catheter reconstruction faster and more precise than the manual one
- Another interesting application is the real-time tracking of a HDR source. Two groups have developed similar methods essentially using a flat panel detector in conjunction with a matrix of markers in a known geometry relative to the panel [42]. The exit dose from a patient is enough to produce images of the markers; each image is paired with its marker and ray back tracing can provide information about the 3D position of the source. Bondal et al. have further developed the method by comparing, in real-time, the planned dwell position of the source with the actual position as retrieved by the intersection of all rays; if the distance becomes greater than a predefined threshold (by the source being placed in the wrong catheter, for example), the treatment automatically stops

Tools for Multi-Modality Imaging

- Brachytherapy, as the rest of radiation therapy, has made the leap from 2D to 3D, from planning based on single modality imaging—traditionally fluoroscopy, US or CT—to multi-modality imaging, verification, and assessment
- Unlike EBRT, where large variations in anatomy are not expected to occur from fraction to fraction, brachytherapy poses specific and challenging problems by placement of applicators which do produce major changes in anatomy (e.g., T&O HDR cervical cancer brachytherapy) as well as major patient posture changes (e.g., from lithotomy to supine)
- In the fall of 2012, Medical Physics hosted an interesting point counterpoint debate on the subject whether "it is not appropriate to 'deform' dose along with deformable image registration [DIR] in adaptive radiotherapy" [43]
- Even when restricting the image sets to H&N patients imaged in the same position with very similar modalities (CT and CBCT), the conclusion is that "in spite of all methods resulting in comparable geometrical matching, the choice of DIR implementation leads to uncertainties in dose warped, particularly in regions of high gradient and/or poor imaging quality" [44]
- In brachytherapy, image registration involves the combination of several image sets/modalities at one time point or multiple image sets from several time points.
  - The most common version of "registration" is reconstruction of applicators (from a library or a previous fraction) followed by propagation of contours from different image modalities and/or time points
  - Dose accumulation is used mostly in relation to OARs and commonly employs "parameter addition" rather than dose warping. Deformable registration in OARs (bladder, rectum, sigmoid) is not used on a regular basis due to large uncertainties and unreliable deformations

- Intra- and inter-fraction movements of the tumor relative to the applicator is limited in cervix intracavitary applications, and therefore registration between image series should always be performed in reference to the applicator, and registration on bone is strongly discouraged
- In prostate permanent seed implant brachytherapy, ultrasound and fluoroscopy have been traditionally used in conjunction: one has good ability to visualize anatomy using a rectal probe but poor resolution in determining seed position, the other allows for very clear visualization of the seeds and needles but has essentially no ability to see soft tissues or interfaces
  - Most often these two modalities are used for qualitative guidance during the procedure and CT is used at a later time to assess the quality of the implant by retrieving the geometry of the implant and segmenting the anatomy
  - Many investigators have worked to refine the quantitative use of the fluoroscopy + ultrasound combination, the main idea being “fusing” or registering, using a system of fiducial markers or the seeds themselves, the ultrasound volumetric dataset with 3D seed positions retrieved from fluoroscopy acquired in multiple poses. With complete information about the anatomy and seed positions, one would be able to retrieve the dosimetry of the implant in near real time

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