Chapter 9

NEW TECHNOLOGY FOR IMAGE-GUIDED THERAPY

Trends and Innovations

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Abstract: Image-Guided Therapy (IGT) uses imaging to plan, implement, and follow-up treatment. Typical goals are personalized treatment planning, accurate targeting, therapeutic effectiveness, decreased procedure time, minimal side effects, and responsive follow-up. Many IGT technologies involve pre-, intra-, and post- procedure stages. Intra-procedure processes include targeting, monitoring, and controlling[1]. Trends and innovations are reviewed for multi-modality-guided percutaneous ablation, catheter ablation for cardiac arrhythmias, MR-guided therapeutic ultrasound, and advanced radiation therapy. These technologies have a role in treatment centers of the future, and will ultimately be measured in terms of improved patient outcomes.

Keywords: Medical trends, medical imaging, diagnosis, image-guided therapy, minimally invasive surgery, HIFU, RFA, radiation therapy, molecular imaging

1. OBJECTIVES OF IMAGE GUIDED THERAPY

The Tricorder, used by Dr. ‘Bones’ McCoy in the Star Trek Sci-Fi series[2,3], was a hand-held, fully integrated ‘Sense-Cure’ device. By hovering the device near the afflicted area, it could both ***sense and cure*** (space-age) ailments in a matter of seconds.

The idealized capabilities of the Tricorder, unfortunately, represent formidable clinical and technical challenges in present day, especially when implying potentially curative outcomes for major chronic diseases such as

G. Spekowius and T. Wendler (Eds.), Advances in Healthcare Technology, 139-146.

cancer, heart disease, and diabetes; nevertheless, some aspects of the Tricorder are being realized in state-of-the-art technology and their advancements.

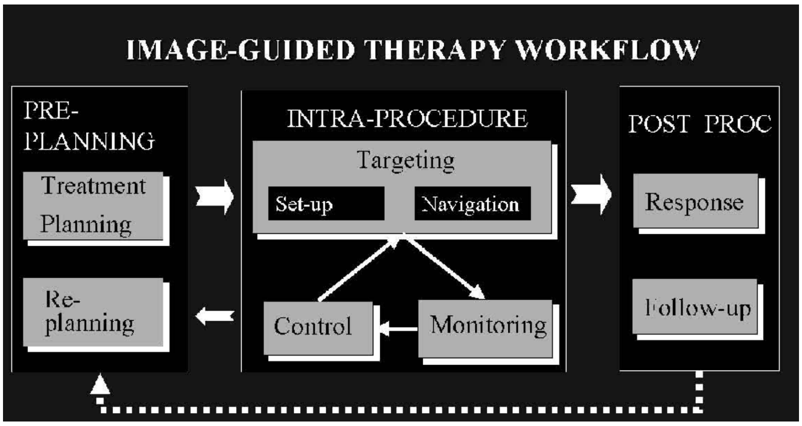

Figure 9-1. Typical 'See-Treat' workflow for many image-guided therapy procedures.

Instead of 'Sense-Cure' capabilities, many state-of-the-art technologies in image-guided therapy seek to facilitate the following objectives (some of which, in an imaginary sense, may be intrinsic to Dr. McCoy's Tricorder):

- Image, accurately detect, and localize the tissue targeted for treatment,
- Quickly develop a patient-specific treatment plan for the target tissue (e.g., in less then two minutes) while minimizing risk to nearby structures and minimizing side effects,
- Quickly and easily implement the plan by accurately targeting the lesion during the procedure with minimal risk, side effects, and ionizing radiation to healthy tissue,
- Directly monitor the treatment's effectiveness in 'real-time' and use this information to adjust targeting and the treatment plan,
- Accurately assess the post-procedure treatment response,
- If the treatment is incomplete or if the original treatment plan for fractionated treatment is no longer valid, then update the plan with re-imaging in some cases.

2. CLINICAL PROCEDURE STAGES IN IGT

Prototypes, concepts, and investigations to meet these image-guided therapy objectives are discussed in the sections and chapters ahead. Each of them typically involves Pre-, Intra-, and Post-procedure stages (Figure 9-1), and the intra-procedure stage typically includes Targeting, Controlling, and Monitoring processes.

These stages and processes are not always clearly delineated; they can overlap and can be iterative. For example, information obtained while monitoring the treatment can be displayed on images from, and used to update, the pre-procedure plan. Another example is that simultaneous planning and targeting processes can be used when repositioning or refocusing devices based on imaging feedback.

3. TRENDS AND ADVANCES IN IGT

3.1 Less-and-less invasiveness

Rapid advances in medical imaging have enabled these IGT objectives and processe to be performed with less-and-less invasiveness. Laparoscopic procedures, via keyholes, are often replacing open surgical procedures; transcutaneous procedures, via extracorporeal delivery, are replacing percutaneous procedures. Less-invasive and non-invasive procedures inherently need tomographic, projection, or sector imaging to increase visualization of the interventional field and target treatment locations.

Extra-corporal, i.e., transcutaneous, non-invasive procedures such as Radiation Therapy, Therapeutic Ultrasound, and Lithotripsy require imaging for *planning* and, in some cases, for intra-procedurally *monitoring* the treatment. Virtual 'Radiation Therapy' (RT) Simulation is now commonly used with large bore, multi-detector row CT scanners. The 3-D coordinates of a solid tumor can be localized online, with digitally reconstructed radiographs (DRRs), immediately after acquiring a multi-phasic CT data set. These coordinates are sent to CT-integrated lasers, which enable the skin to be marked for subsequent positioning on a LINAC. Methods are under investigation to decrease inaccuracies of the RT due to respiratory motion and organ shift (Chapter 13). A retrospectively gated CT scan can be used to include respiratory motion in the therapy planning stage. Also, improved model-based segmentation algorithms are being investigated to further automate *planning* processes, and help to more accurately predict doses to targets and critical structures.

In MR-Guided Therapeutic Ultrasound, i.e., High-Intensity Focused Ultrasound (HIFU) (Chapter 12), the MR scanner provides both a 3-D anatomical map and 'thermometry' to *monitor* and *control* heat delivery. Treatment of uterine fibroids with MR-guided HIFU has recently been FDA approved. Diagnostic Ultrasound, registered with 3-D CT data, is also being investigated for *targeting* and *monitoring* HIFU therapy (Chapter 10).

3.2 Endoscopy often replaces open surgery

Many image-guided treatments cannot presently be administered extracorporally. Continuous and pulsed HIFU is being investigated for ablation and local drug-delivery within the liver; but, these techniques may not be applicable when high frequency acoustic energy cannot penetrate to the target tissue or when direct manipulation of tissue is needed.

Endoscopic surgery was first used in the late 1970s and a significant amount of training was required for obstetric and gynecology physicians. After being adopted for gall bladder resection in the 1980s, laparoscopic surgery was extended to the appendix, spleen, colon, stomach, kidney, and liver in the 1990s. Robotic assistance for remote endoscope manipulation was introduced at this time, but has been slowly adopted, potentially due to its high cost and marginal value for well-trained surgeons.

Endoscopic examinations of the colon, i.e., colonoscopy, – with on-line polyp resection – is today one of the most successful examples of an integrated, non-invasive approach to screening and diagnosis combined with minimally invasive therapy.

Multi-modality imaging is being investigated to enhance abdominal laparoscopic procedures. A miniature electromagnetic sensor (Chapter 10) is attached to the tip of an ultrasonic laparoscope and registered and tracked in a recently acquired 3-D tomographic data set. Combining real-time imaging, e.g., ultrasound, angiography, MR or CT Fluoroscopy, with the 3-D retrospective data sets is an emerging concept in multi-modality image-guidance (see below and Chapter 10).

Another recent innovation in the area of endoscopy is the integration of imaging and non-invasive therapy using a pill-sized endoscopic capsule, first introduced in 2001. Current models are 1 cm x 2 cm and can wirelessly capture 0.4 megapixel video at up to 30 frames/second. In the future, these capsules could have a remotely controlled camera direction, take tissue samples, and deliver medications – like a telemetric version of Asimov's '3 micra' submarine, Proteus, in the Fantastic Voyage[4].

3.3 New procedures for the cardiac cath lab

Using fluoroscopy during interventions, to track minimally invasive instrument-based intervention, has lead to the growing discipline of Interventional Radiology and the exponential growth of catheter-based procedures, which – together with the availability of ever more complex stents - have since steadily replaced open surgery in the heart, abdomen, and brain, to name the most important areas. The 'Catheter Lab' developed into a truly integrated approach to diagnostic imaging and therapy.

Complex procedures are performed today in the Electrophysiology (EP) laboratory (see Chapter 11) to interrupt arrhythmia-causing nerve conduction with highly accurate catheter-based ablation while *monitoring* ECG signals. The catheter tips carry tiny electromagnetic coils for accurate non-line-of-sight localization. Cone-beam CT data sets are being investigated to assist EP 3-D treatment *planning* and for intra-procedure registration with the real-time Angio imaging, and MR-guided EP procedures are also under investigation.

3.4 Multi-modality guidance and molecular imaging

As with combining real-time imaging with retrospective data sets, there is, more generally, an increasing trend of inter- and intra- modality registration in both diagnostic and therapeutic imaging. As an important example in diagnostic imaging, Positron Emission Tomography (PET) and Single-Photon Emission Computed Tomography (SPECT) are now integrated and share a patient table with CT imagers. Furthermore, CT and MRI anatomical imaging is also being complemented with functional MRI (brain activity, metabolism in MR-spectroscopic images, and diffusion imaging). These and other hybrid imagers enable the registration of 3-D morphological images with functional imaging of molecular processes and pharmakinetic/dynamic properties of new agents. Examples include imaging of metabolism, apoptosis/inflammation, angiogenesis, anti-angiogenisis, and immunological processes. In the new paradigm of Molecular Imaging (MI), these imaging modalities (and also optical and ultrasound imaging) are used in combination with molecular contrast agents[5] which are targeted to disease-specific proteins and receptors, thus providing enhanced image signals from the pathology.

Registration and fusion of multi-modality data sets to plan Radiation Therapy or Surgery is presently available. In oncology, further use of multi-modality imaging could enable: The accurate delineation of heterogenous tumors for image-guided percutaneous ablation (Section 3.5), perfusion visualization for targeted drug delivery with HIFU, or more accurate tumor targeting with image-guided radiotherapy (Chapter 13) or particle beam therapy. Many new approaches combine targeted drugs with contrast agents, such that a real-time 3-D imaging modality can be used to monitor the distribution and localization of a therapeutic agent as it delivers its payload. Multi-modality molecular image approaches are also being investigated for monitoring the response to radiation therapy (Chapter 14).

3.5 Interventional oncology and percutaneous ablation

The first CT guided biopsy was reported by Dr. John Haaga in 1976[6]. Radiologists' have since typically become relatively skilled at placing needles with CT or Ultrasound (US) guidance for percutaneous biopsies and fluid drainages. Some needle-based procedures involving double angles, deep targets, and targets near critical structures or the diaphragm, however, may pose more challenges. These may require more use of real-time imaging and breath-hold reproducibility techniques.

The transition from needles to Radiofrequency electrodes for percutaneous ablation of hepatic tumors was first suggested in 1990[7,8]. Since then, the technique has rapidly expanded to treatments of other areas such as kidney, lung, and bone tumors, and has developed into a new field of 'Interventional Oncology'.

The leading RFA application has been the treatment of solid liver tumors, especially indicated when these are un-resectable. Presently, tumors larger than 3 cm can be difficult to treat, without risking marginal recurrence, due to the potential difficulty of placing multiple electrodes to cover the tumor. Innovations being investigated to meet this challenge include: point-and-click treatment planning and simulation with virtual electrodes, targeting with CT-integrated robots, electromagnetically tracked electrodes, and CT-Ultrasound image registration (Chapter 10). Heat-activated drug delivery during RFA is another recent method being investigated to combat marginal recurrence.

An example of personalized medicine in the post-genomic era aims to use proteomic and genomic analysis of biopsy tissue samples to evaluate drug effect and investigate tumor genetics. This requires a biopsy sample of a heterogeneous tumor at precisely the same location pre- and post therapy. New devices such as a CT-integrated robot with inter- and intra-modality image-based planning, as discussed in Chapter 10, may facilitate more reproducible sequential biopsy sampling. Eventually, molecular imaging may alleviate the need for biopsy in the process of developing personalized medicines.

3.6 Real-time imaging and virtual tracking

In the mid 1990s, 'frameless stereotactic' approaches were developed for the operating room using optical (line-of-sight) navigation systems (Chapter 10). After registering the surgical tool, the operating field, and the image-space coordinates, the optical camera enabled the tracking of a surgical tool within a pre-operative CT or MR data sets.

A prerequisite for sufficient accuracy in these approaches was the proper correction of geometric distortions, which are inherent not only to MRI (dependent on acquisition protocol and anatomical area), but to some extent also in CT image data. Also, navigation in static CT or MR data sets, as a form of virtual reality, did not reflect intra-procedural, morphological changes in tissue. Accordingly, applying frameless stereotactic techniques to the areas such as the lung and abdomen can pose challenges due to respiratory motion and organ shift/deformation. This can be mitigated with the use of real-time imaging in combination virtual tracking of instruments in recently acquired image data sets (Chapter 10).

In view of the X-Ray dose to both patients and clinicians during fluoroscopy, attention is increasingly being paid to alternative fluoroscopic imaging modalities such as 3-D ultrasound and MRI. In this context, recent advances in the real-time localization of MR-microcoils have paved the way for integrating catheter or instrument localization with the MR data acquisition.

Also, new visualization methods and dose mitigation strategies are being investigated for volume CT-fluoroscopy (Chapter 10). CT-integrated robots are being investigated to remotely steer interventional devices during real-time Volume (3-D) CT-fluoroscopy imaging.

4. SUMMARY

New technologies for image-guided transcutaneous, percutaneous, and endoscopic procedures will be reviewed in the following chapters. In the future, the ideal treatment paradigm would enable the multi-modality (including molecular) image-based treatment planning, guidance, monitoring, and controlling of treatment effectiveness in one seamlessly integrated platform. Imaging, tools, and devices can be easily accessed before and during the procedure to simplify workflow, within and between stages, to achieve the therapeutic objectives.

Trade-offs often exist between approaches, associated tools, and alternatives, and these depend on the application and venue. For example, real-time imaging can increase targeting accuracy and decrease the procedure time; but the use of ionizing radiation may require strategies to decrease x-ray dose to the physician and the patient. Registration and real-time tracking of interventional tools in a static 3-D data set may provide real-time navigational feedback in virtual reality space, but may not always be a sufficient substitute for continuous or intermittent fluoroscopic imaging of the interventional field and surgical devices.

With some image-guided applications, the clinical protocols and technical methods are under varying stages of clinical investigation. There may be multiple approaches to achieve the same therapeutic objectives and they can have complex trade-offs. Clinical protocols and use of technology may vary between, or even within institutions, and always depend on the presentation of each patient. For instance, there are presently at least seven types of chemical and thermal energies used to destroy tumors, e.g., RFA, laser ablation, alcohol installation, cryogenic, etc. These are often used in combination with other treatments and are the subject of many international studies[9].

For a new device, imaging method, or procedure to be accepted or embraced by the clinical community, it must be of significant benefit without adding cost, time, or the need for a non-trivial amount of training. For some procedures, this may first occur in less challenging regions such as those easier to target and monitor. Interdisciplinary teams, e.g., researchers, surgeons, oncologists, interventional radiologists, and cardiologists, must work synergistically to understand and re-visit requirements associated with the new devices.

The Star Trek Tricorder is not light-years away. Ultimately, here on earth, the value of IGT technology will be always measured in terms of a better outcome for the patient.

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