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THE PROCESS AND DEVELOPMENT OF IMAGE-GUIDED PROCEDURES

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■ **Abstract** Medical imaging has been used primarily for diagnosis. In the past 15 years there has been an emergence of the use of images for the guidance of therapy. This process requires three-dimensional localization devices, the ability to register medical images to physical space, and the ability to display position and trajectory on those images. This paper examines the development and state of the art in those processes.

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MOTIVATION FOR IMAGE GUIDANCE

One of the most fundamental forces in the development of surgery and other forms of directed therapy is the need to increase the information available to physicians and to place that information in both spatial and temporal contexts. From such perspectives, the development of surgery, radiation therapy, and now even chemotherapy can be followed. In each field, there is a movement to finer and finer preoperative determinations of pathology locations coupled with intraprocedural determinations of therapeutic positions. This process can be seen as progression from providing therapy to a general patient to treating a specific one.

In all therapies, what is needed for successful outcomes is knowledge of the spatial location and extent of a problem. To use surgery as an example, with the advancement of surgical techniques came the need for a surgeon to exactly define the location of his or her instruments. Simple visual inspection gave way to magnifying loupes, loupes to operating microscopes and endoscopes. This relationship between knowing the spatial location and extent of a problem and performing the surgery is so intuitive that only eight days after the announcement of Roentgen's discovery of X rays, the first image-guided surgery was performed. On January 13, 1896, a woman in Birmingham (UK) buried a needle in her hand. A radiograph was made of her hand, which she took to casualty surgeon JH Clayton to help him in his surgical removal of the needle (1). Here the trauma was known, the shape and size of the surgical target exactly defined. The radiograph reduced the uncertainty of the location of the needle relative to other anatomic structures in that patient. However, because simple radiographs compress three-dimensional spatial relations into two-dimensional images, there remained a degree of positional uncertainty relative to the thickness of the patient's hand. In addition, a radiograph shows only the bony anatomy clearly; therefore, the surgeon's knowledge of the location of other structures, such as tendons and vessels, was still dependent on his understanding of general anatomy.

This same progression can be seen in other therapies as well. Simple external beam, quadrant-directed radiotherapy has been enhanced by stereotactic radiosurgery and therapy; brachytherapy delivers radiation from the inside of the tissue outward; and direct-injection, controlled-release chemotherapy is replacing systemic chemotherapy in certain applications.

As imaging has progressed from simple, static X rays to include tomograms and dynamic imaging, the application of those images to therapy has moved with it. As image sets became three dimensional in space and time, the technological complexity of putting them to use increased dramatically. This necessitated the creation of physician-engineer teams to develop devices and techniques, a collaboration that has grown to become the field of image-guided procedures (IGPs).

Because preinterventional images exist for the vast majority of therapeutic procedures, what constitutes an IGP? One definition is that in an IGP, images are used quantitatively. That is, their spatial parameters carry equal or greater weight than their gray-scale parameters. Thus, the mere presence of tomographic images in an operating room, or the use of intraoperative imaging to visually align tool and target, does not, by this definition, create an IGP.

HISTORY

Approximately 10 years after the surgery by Clayton (1), Horsley & Clarke (2) presented a device that embodied two ideas fundamental to surgical guidance: image space and physical space. For their process, known as stereotaxy, to work, both the image space and the physical space must in some way be registered, i.e. the transformational relationship between two three-dimensional spaces must be determined. In this case the image-space map consisted of anatomic drawings and sectioned samples, but it inaugurated the concept that direct surgical visualization was no longer necessary for the accurate placement and guidance of medical devices. Their concept for charting the physical space was an extracranial device, or frame. Horsley & Clarke accomplished this by mounting on a subject a frame based on intrinsic reference points, anatomic landmarks, such as the external auditory canals and the inferior orbital rims. Based on these landmarks, the frame could be identically mounted on every subject and the image-space maps could then be used to place electrodes, make lesions, and take tissue samples. There is an implied relationship here: that intracranial structures of the brain have a stationary relationship to extracranial anatomic landmarks across the subject population. That is, the general case sufficiently defines the specific. However, the fundamental problem in using this technique on humans was that the map between external anatomic landmarks and intracerebral locations proved not to be stationary across human beings. Thus, for accurate guidance, generalized atlases and representative tissue sections alone were inadequate.

Although stereotactic techniques have been applied to a number of different surgical areas (3–6), stereotaxy has found its most common application in neurosurgery because of the singular structure of the cranium. The need to operate on this structure, unique in that it is a solid organ almost entirely encompassed by bone, leads to two major constraints. The first is with the protective nature of the skull. Surgeons prefer to make the minimum opening required to perform the surgery but must make a large enough opening to guarantee access to the entire site. Second, there is the functional importance of all the tissue between the surface of the brain and the site of surgical interest. These surgical constraints have led to a desire to develop techniques for accurate location of positions within the brain prior to the opening of the skull.

The term site of surgical interest is meant to span all the applications of stereotaxy. The first, and still most-often used, application of stereotaxy was for the placement of electrodes to known physical locations for the mapping of the brain's electrical activity and functional response (7–12). The mapping process was followed by the development of surgery that attempts to change the function of the brain in some fashion. These procedures, collectively known as functional neurosurgery, differ from other forms of stereotactic neurosurgery in that there is not always a visible focus for resection, and the surgery is not to remove some lesion or vascular abnormality but to attempt to change some undesirable neurologic function. The surgical point is determined by observation of the local area's function, generally through electrical monitoring, and the correlation with known functional locations or anatomic landmarks.

In 1947, Spiegel & Wycis (13) published a paper describing their device for human stereotaxy. This apparatus did not use skull landmarks for the location of soft-tissue targets. Rather, it extracted information from pneumoencephalograms. By providing visual information as to the relationship between the stereotactic apparatus and soft-tissue landmarks, such as the foramen of Monroe and the pineal gland, electrodes could be guided with much greater certainty. By taking care to preserve well-defined geometries in their imaging, each patient's films became a specific atlas to guide electrode placement. In addition, it is an example of the use of image information in a quantitative way. Arguably, the concept of using pneumoencephalograms and ventriculography as a mapping of the topology of the brain did not occur to Spiegel & Wycis exclusively. During the next few years, several major stereotactic systems were initiated. This included the first Leksell (14) and Riechert & Wolff (15) (later Riechert-Mundinger) systems. In France, Talairach et al (16) returned to Horsley & Clarke's electrophysiology idea by using anatomic landmarks and an atlas of function combined with patient-specific information from images to allow the placement of electrodes. Two reviews of stereotaxy can be found elsewhere (17, 18).

With general charts proving to be unacceptable, stereotaxy had to await an improved method for determining locations within the brain. The development of pneumoencephalograms and, later, iodine-based contrast agents for ventriculography started the process of patient-specific localization. Now structures within an individual's brain could be visualized, and landmarks and distances determined for each subject. A surgeon could visualize specific anatomy in his patient. The use of radio-opaque materials for constructing the frame allowed it as well structures within the brain to be seen in the images. But the pneumoencephalography/ventriculography technique was not without its drawbacks. Because both types of images are shadowgrams, or projection images, they compress information about a three-dimensional object onto a two-dimensional plane. If a point could be uniquely determined in both anterior-posterior and lateral films, then a probe could be guided to that point by a series of frame adjustments. The ability to exactly define the point of surgical interest in both films was in no way guaranteed. In the absence of exactly definable points, the surgeon's experience and knowledge of general anatomy could help approximate the site of surgical interest, the general case combined with specific information helping to better approximate the individual case. If the target were visually or electrically distinguishable from the rest of the anatomy, then the site's location could be refined from the rough position determined by the frame. The conceptual breakthrough was that the ventriculogram provided surgeons with patient-specific information to modify their three-dimensional understanding of general neuroanatomy.

Once localization and targeting techniques had been developed, stereotactic methodologies were invented for a variety of therapeutic procedures. As was the case with the electrode placement, therapeutic protocols followed protocols designed to gather information. Once it had been shown that a narrow-guage needle could be placed at the tumor site with relative accuracy, local radiation therapy by the stereotactic placement of radiation sources became possible (19, 20). Currently, there is an array of different radioactive materials that may be placed at the target site (21–24). To some degree, different materials are selected for different tumor types, so the biopsy procedure often precedes placement. Recently, there has been an expansion of interventional efforts to place therapeutic objects directly in the lesion. These include controlled release chemotherapy agents (25).

When assessing the efficacy of chemotherapy and radiation therapy protocols for deep-seated tumors, histologic confirmation of the neoplasm type is desirable. Furthermore, biopsy may be pivotal in the selection of the most appropriate course of treatment. Surgical biopsy by craniotomy subjected patients to most of the risks of surgical resection. Stereotactic biopsy was developed as a greatly less-invasive procedure for capturing tissue for histological examination (26–30). Once the neoplasm type is exactly defined, then the most appropriate form of therapy can be prescribed.

Along with aiding in resection, in which tissue is removed from the brain, stereotaxy can aid in transplanting tissue into the brain. The transplantation of adrenal medullary tissue into the brain for the alleviation of Parkinson's disease symptoms is a surgical procedure of both great promise and great debate (31–33). One factor that has led to the uneven success among various sites is the variability of the implant location. Stereotactic techniques can be used to control that variability, helping to place implants of glandular tissue in specific, consistent locations, thus reducing the risk of the procedure.

Stereotactic techniques were also developed for external beam radiation. In 1951, Leksell (34) introduced the concept of radiosurgery, i.e. the use of targeted external beam radiation, in which the dose delivered to the target is built by the summation of beams from a variety of angles. This method allows a greater dosage to be delivered to the target while reducing that to the rest of the tissue. Modern tomographic methods have allowed better definition of tumor margins, and new techniques for intensity-modulated radiation therapy allow for the "sculpting" of the delivered dose (35, 36).

ADVENT OF IMAGE-GUIDED PROCEDURES

The creation of computed tomography (CT) provided the surgeon with a three-dimensional, patient-specific atlas. Although a number of researchers used this new technique with frames (37–40), and techniques were developed to merge CT and plane film data (41), the availability of three-dimensional data coupled with a rapidly advancing computer field made new approaches possible. In the mid to late 1980s, a number of researchers began to develop systems that, although varying greatly in implementation, shared a common revolutionary idea: track the surgical position in the physical space and display position in image space. This constitutes a reversal of classic stereotaxy, in which the physical location is determined from the images. Dubbed frameless stereotaxy by some (42–44) and interactive, image-guided neurosurgery by others (45, 46), the process had three major components:

1. A three-dimensional spatial 1ocalizer. This device could be freely moved in the operating room, and the location and trajectory of its tip dynamically tracked. Thus, the device would return a position triplet $\langle xp, yp, zp\rangle$ for the space defined by its motion.
2. A registration technique. As with previous stereotaxy, the relationship between the space defined by an extracranial device and locations seen in the image space $\langle xi, yi, zi\rangle$ must be determined. Instead of mapping image location into frame adjustments, $\langle xi, yi, zi\rangle \Rightarrow \langle xp, yp, zp\rangle$, the 1ocalizer position is mapped into image space $\langle xp, yp, zp\rangle \Rightarrow \langle xi, yi, zi\rangle$ and that point is displayed on the appropriate image or images. This means that all image information is retained and dynamically displayed as the surgeon moves the localizer. Thus, surgeons are able to determine not only their present surgical position but the position of all perceptible anatomic structures.
3. A means of displaying the location in image space. The timing of the development of systems that tracked surgical location in image space was not accidental. Computers capable of storage, recall, and display of large medical image sets, and yet of a size and cost appropriate for operating rooms, were not available until the 1980s.

The first system in press was the tracked microscope system of Roberts et al (47, 48) from Dartmouth, followed quickly by a system developed in Tokyo (49, 50). It is appropriate that the first two systems used two distinctly different methods for surgical location. The Dartmouth system used a sonic triangulation method for localization, whereas the Tokyo system used an articulated arm. Those two approaches represent the dominant three-dimensional localization paradigms, as explained below.

FUNDAMENTALS OF IMAGE-GUIDED PROCEDURES

IGPs have four basic components: image acquisition, image-to-physical-space registration, three-dimensional tracking, and display of imaging data and location. In addition, some registrations and displays require segmentation techniques.

Image Acquisition

IGPs require dealing with five different types of images:

1. Projective images such as plane films and angiograms; tomographic sets such as computed tomography (CT), magnetic resonance imaging, (MRI), and emission tomograms (SPECT, PET).
2. Intraoperative two-dimensional imaging; ultrasound image, which creates slices but which a number of researchers are combining into volumes.
3. Laparoscopic, endoscopic, and microscopic images, which are projective and may have distortions; intraoperative plane film imaging, which is both projective and has distortions associated with the image intensifier.
4. Intraoperative tomograms, including both CT and "open-frame" or "therapeutic" MRI.
5. Processed images, including rendered images that may represent an extracted anatomic surface, and images such as maximum intensity projections from tomographic angiograms.

Although the history of stereotaxy is dominated by projection images, in IGP they are rarely used. This is due to two issues. First, in order to form a registration, six reference points (fiducials) are required to be located in image space and physical space. Tomograms require only three to be found (51, 52). Second, a projective image has significant spatial uncertainty in the third dimension.

At Montreal Neurologic Institute, there is a history of the acquisition and use of stereo pair angiograms (53). This history carried over into the stereotactic and IGP system developed there (54, 55). By obtaining stereo images, the depth uncertainty can be reduced. That simultaneously obtained projection images can reduce spatial uncertainty has also been shown with "C-arm" intraoperative imaging and fluoroscopy (56). The pincushion and S distortion in the image intensifiers can be corrected (57), and if homologous points can be unambiguously identified in both images, then the point can be identified in three dimensions.

Tomographic scans have been used since the initial development of IGP. Both Roberts et al (47) and Watanabe et al (49) displayed surgical position on a single tomogram slice. Galloway et al (58) demonstrated a four-window display (each 512 × 512 pixels) with image sets selectable from various tomographic modalities. These images could be displayed in the native orientation, or reconstructed sets in the other cardinal planes could be shown. Guthrie (59) and Smith et al (60) developed systems in which the original image volume was resliced to show the plane perpendicular to the surgical trajectory. Perhaps the first real demonstration of the power of using modern tomographic sets quantitatively was in a surgery performed to separate conjoined twins (61). Here the data was used not only for qualitative assessment and point localization, but also for distance, surface, and volume determination. Although these results were not directly linked to the procedural guidance, the success of the procedure demonstrated the true value of image analysis, image processing, and data extraction in guiding a therapeutic process. These processes allowed the determination of the volume of shared tissue and the amount of skin needed for grafting and allowed surgeons to simulate different approaches and resection strategies.

There are two major difficulties of using preoperative tomograms as an exclusive form of guidance. The first is that the tomogram requires that the surgeon look up from the surgical view and blend it with the tomographic orientation. This difficulty has been addressed in a number of ways. In 1993, a concept called enhanced reality was pioneered, in which rendered objects from a tomographic data set were projected into the surgical viewpoint and blended into the visual display (62, 63). This concept was furthered by injecting that blended image into an eyepiece of a surgical microscope (64). There are significant challenges to these systems in terms of not overwhelming the visual system of the viewer.

Mainwaring (65) pioneered a different approach in which a tracked endoscope serving as a surgical pointer had its position displayed on a computer monitor. By placing the computer monitor showing the tomographic position next to the video monitor showing the endoscope images, the data from each could be merged. Stefansic et al (66, 67) have shown derivative systems in which the video images replace one of the windows in a four-window display. A related but distinct approach uses an image set derived from a tomogram set. In virtual endoscopy (68, 69), a tomographic set of anatomical structures able to be traversed by endoscopes is segmented and rendered in such a way that a path mimicking that of an endoscope can be followed. This has the advantage that, unlike with a true endoscope, it is possible to see "beneath" the surface of the tissue of the traversed structure. Such a virtual endoscope is also able to get past blockages that may foil a true endoscope. However, such displays cannot provide the visual clues as to whether tissue is healthy or not. Therefore, the combination of virtual-endoscopy and true-endoscopy images retains the power of both methodologies (70, 71).

Three-Dimensional Localization Systems

Localization technologies can be divided into three classes: geometric, triangulation, and inertial. Although there have been some attempts at using inertial systems for surgical localization devices, currently such systems are unwieldy. The primary confounding property of the localization task is that it is actually a six-dimensional task. To be of real use, not only the X, Y, and Z axes but also the spatial orientation of a device must be tracked. These orientations can be represented as Yaw, Pitch, and Roll. Certain geometric techniques, such as placing the device tip along a device axis, can reduce the problem to five dimensions, but for inertial systems that still means five gyroscopes or gyroscope-equivalents.

Thus, the field of localizers can be reduced to two classes of devices: geometric and triangulation. As mentioned above, these two classes were represented by the first two IGP systems, the Dartmouth and Tokyo systems. Geometric localizers use angle, extension, and/or bend systems to sense the position of the procedural device.

Articulated arms using potentiomenters or optical angle sensors are the most common. Beyond the Tokyo system, researchers from the University of Aachen (72), Vanderbilt University (73), the University of Oolu (74), the University of Alabama-Birmingham (75), and Henry Ford Hospital (76) all developed systems using articulated arms. In addition, one of the first commercially available systems from ISG used an articulated arm made by Faro Technologies (Lake May, FLA) (77).

Articulated arms suffer from one major problem as surgical localizers: In order to be accurate, they must have stiff arms between the rotational joints. That requirement limits how light the device can be. And although counter-weighting can make the device's end effector seem to float, such techniques add to the mass and, thus, to the inertia of the device. It is because of this constraint that most developers have moved away from articulated arms as surgical localizers. They may yet have applications in nonsurgical IGPs, such as positioning patients for radiotherapy.

Although the use of articulated arms is on the wane for image-guided surgeries, there is a growing application for another geometric localization technology. In a number of therapeutic procedures, for example otolaryngology and colon polyp biopsy and treatment, it is difficult or inappropriate to use rigid instruments. Technologies such as the Shape Tape™ allow the tracking of curvature and, thus, the end point of the devices (78). Although the accuracy of such systems is not what it needs to be for IGP, active development is under way.

The second major type of localization systems used in IGP is triangulation. In these systems, an emitter or emitters broadcast energy to a series of detectors at known locations. By measuring the distance or angular position of the emitters, the emitter's location can be determined. If three or more emitters are mounted on a rigid structure, then the location and orientation of that structure can be determined.

In the pioneering work done at Dartmouth (48) and the in later work done at the Cleveland Clinic (79), the triangulation systems were sonic. They consisted of emitters mounted to the microscope (Dartmouth) or to a bipolar cautery device (Cleveland Clinic). In both systems, multiple spark-gaps were used as a sound point source and the time-of-flight (TOF) between source and detector was measured. From this, the distance was determined and the location triangulated. The acoustic systems had two problems, both related to the speed of sound. Variations in the speed of sound led to errors in the determination of the emitter location and, thus, the object's location. This could be handled by a method called pilot sparking (80), in which a fixed spark gap was fired periodically and variations in transit time were used to correct for changes in the acoustic propagation velocity. The second, and more intractable, problem was that of TOF. In the time from the first event to the last, the device cannot move or a serious localization error will occur. Therefore, the device must remain stationary for N (TOF + TD), where N is the number of emitters and TD is the timing delay between spark events necessary to deal with reverberations. If you presume an average emitter-detector distance of 2 m, then the TOF from each emitter to the detector (in standard temperature and pressure) is 6 ms. This requires a stationary tracked object and limits update rates and numbers of emitters, thereby making the device sensitive to shadowing (81). Shadowing occurs when the handle of the device lies between the emitters and the detector, thus blocking localization.

The TOF issue vanishes if the ultrasound energy is replaced by electromagnetic energy. With electromagnetic sources, TOF and TD effectively become zero replaced only by source and detector time constants. This means that in directional sources, such as optical sources, the number of emitters can be high, allowing for full range of motion without object shadowing. If the electromagnetic emitters are radiofrequency (82) or magnetic (83, 84), which are effectively omnidirectional, then the only limitation on the number of emitters is their size.

Optical devices, both active (84–86) and passive (87–89), currently dominate the IGP field. This is perhaps surprising, given the need for a continuous line of sight and the directional restrictions of the optical emitters that either force a large number of sources or limit the orientation of the tracked device. However, optical methods may be winning by default. The surgical suite contains large, conductive structures, such as the operating table. Because of the motion of tools and conductive fluids, and the presence of electrically active devices, such as abalators, imaging devices, and patient-monitoring equipment, it is a dynamic, conductive environment. All these factors (90) confound radiofrequency and magnetic localizers. Active work continues on magnetic localizers (91), especially for tracking devices in closed-patient situations where it is impossible or impractical to maintain a rigid, visible device.

REGISTRATION

Three-dimensional localization and tracking devices determine position in physical space. In order to use that information quantitatively with image data, a registration from image space to physical space must be performed. There are three classes of registration techniques: point based, feature based, and volume based. Of the point-based registration, there are two subtypes. The first uses anatomic landmarks or features as intrinsic reference points, or fiducials. The second requires the attachment of extrinsic objects, or fiducial markers. The differences between marker-based and feature-based registration are relatively clear. Because the markers must be in place prior to the acquisition of images, the decision to use marker-based registration must be made before acquisition. For this reason, marker-based registration is said to be a prospective method. In contrast, feature-based registration can be retrospective, meaning that the decision to perform registration can be made after the image sets are acquired. However, feature-based registration, in general, requires more computation than do marker-based methods, and they are prone to larger error (92). In addition, it is difficult to determine the quality of a registration arising from a feature-based registration. In contrast, there are statistical methods for estimating the quality of a marker-based system.

Point-Based Systems

In point-based systems, points are localized in both image space and physical space. The locations of these landmarks in the two spaces can be arranged as lists of three-dimensional coordinates and a three-dimensional transformation between the two sets determined by any one of a number of mathematical methods (93). In the early image-guided surgery systems, anatomic landmarks, such as the nasion, the tragi, and the orbital rims, were used as intrinsic fiducials (49, 77, 94). There are significant difficulties with this approach. It is difficult to define an anatomic point, and even could such a point be located in physical space, the averaging effect of finite-slice thickness introduces a spatial uncertainty. Evans et al (95) demonstrated that by overdetermining the problem, e.g. by localizing more points than the minimum number necessary to determine the transformation (three for three-dimensional images), they were able to produce transformations that were more robust to errors in the localization of any given point. However, if the localization errors among markers or features are uncorrelated, then overdetermination, as, for example, in Evans's approach, can be employed to attenuate the effect of those errors on the calculated transformation.

The benefit of increasing the number of homologous points leads to a challenge in the use of anatomical landmarks. The reason that images of a patient are acquired in multiple modalities is that they provide distinct information. Therefore, almost by definition, it will be difficult to accurately locate a large number of homologous anatomic landmarks in multiple sets. In fact, as the number of modalities increases, the ability to find the same anatomy in each decreases dramatically. Furthermore, in a given modality, the $N + 1$ landmark can always be expected to be more difficult to localize than the N landmark.

In physical-space localization, these same problems arise. As with image localization, if the localization errors are uncorrelated, they can be minimized by overdetermination. However, in attempting to localize significant numbers of points, it quickly becomes difficult to continue to determine structures that can be adequately localized in both image space and physical space. Significant work has gone into using landmarks on the upper row of teeth (96), but they are poorly visualized on MRI and not at all in positron emissions tomography.

The need for large numbers of landmarks arises because of the difficulty of accurately localizing a single landmark. An alternative approach is to construct a landmark, or "marker," that is designed specifically for accurate localization and then to attach it to the patient. Such markers are termed fiducial markers. In using anatomic landmarks as fiducials, researchers attempted to use them as intrinsic reference points. The difficulty is that there are very few anatomic points, and even in those structures that might come to a point, the partial volume effect of tomographic imaging blurs their location into a voxel-sized resolution cell. The difficulty is that the user has only general a priori knowledge about the object he or she is attempting to localize. This handicap severely limits the mathematical tools that can be brought to bear to improve spatial localization to less than a voxel size. However, if there is knowledge about a structure and understanding of how the imaging process works, then the object can be localized in space to a much higher accuracy.

Most researchers developing systems for IGPs have used extrinsic fiducials at some time. Common early practice included surgical staples or small ball bearings for CT (97, 98) and capsules filled with oil or fat for MRI (99). However, the staples caused slight star artifact in CT, making it difficult to localize a part of the staple for use in identification in physical space, and the center of the ball bearing, although easy to localize in image space, was difficult to localize in physical space. The oil-filled and fat-filled capsules exhibited chemical shift of up to 1 cm in the MRI unit, making them inappropriate for localization tasks (100).

As the concept of extrinsic fiducials grew, the physical objects (fiducial markers) that embodied the fiducials became more sophisticated. The markers could be made visible in multiple image modalities, and the mechanisms by which physical space localization was accomplished increased in accuracy. From simple, in-house–created objects to commercially developed and marketed marker systems, a number of fiducial markers are available. In general, they break down into one of two classes: skin-surface attachment or bone-implanted markers. The division between the classes is clear: Skin-surface markers are much less invasive than bone implant markers, but the skin-surface markers contain a potential source of error due to skin motion. This motion may be normal to the skull surface, due to skin swelling or skin drying, or it may be tangential, due to tractions, such as placing the head in a Mayfield head clamp prior to surgery (101).

There are two commercial realizations of bone-implanted markers: the Acustar system, developed by Vanderbilt University and Johnson & Johnson Professional Inc (102), and one developed by Leibinger (103), now a part of Stryker Inc. Implantation of the bone-implant markers is analogous to minor dental surgery. The skin surface is cleaned, and a local anesthetic is applied to the scalp. A small incision is made, and the marker posts are screwed into the outer table of the skull. In the case of the Acustar markers, a flat-bottom hole is drilled and the mounting post screwed into the hole. In the case of markers from Leibinger, the markers mount on a self-tapping titanium post that is screwed into the outer tablature of the skull. The Acustar imageable markers are cylinders, 7 mm in diameter and 5 mm high, filled with a water solution containing iodine and gadolinium, designed to be visible in CT and a wide range of MRI sequences. The size guarantees that at any orientation, the marker is visible in more than one tomogram slice of thickness less than 5 mm. To date, these markers have been tested with T1-, T2-, and proton-density–weighted spin-echo sequences as well as magnetic resonance angiography and gradient-echo images, and they are accurately localizable in all of them (104). The Leibinger marker system consists of a titanium screw, a base component, and an imaging marker. The imaging marker has a 2-mm–diameter spherical volume, which can be filled with a contrast agent. A more complete review of markers is available in a paper by Fitzpatrick & Galloway (105).

Feature-Based Systems

The retrospective nature of the use of intrinsic features continues to appeal. Although difficulties in identifying anatomic points remain, by localizing surfaces or features, the need for one-to-one correspondence is removed, and the use of a large number of points creates an averaging effect that reduces uncorrelated localization noise. A number of researchers have tried to use skin-surface information, both by contact (106) and by optical means (107, 108). The problem with these techniques is that the skin surface is a dynamic structure, responding to both preoperative drug regimens and intraprocedural tractions. For the head, this problem has been addressed by using the skull surface as a registration feature, capturing intraprocedural data by use of a tracked A-mode transducer to localize the skull surface transcutaneously (109). Others have used features on the brain surface for intraprocedural registration (110, 111). However, the brain changes shape once the skull is opened, with the greatest changes being at that opening (112).

For applications other than intracranial, surface information has been used more successfully. Two groups (113–115) have examined surface registration in the spine, either by touching points on the vertebral surface or by tracked, transcutaneous ultrasound. In addition, two groups have used the organ surface in liver surgery (116, 117). A point-based registration is usually used to provide an initial estimate for the surface registration.

The most common algorithm for matching a cloud of acquired points and a derived surface is the ICP (iterative closest point) (118). One intriguing aspect to this method is that a mix of surface and point features can be used. Maurer et al (119) demonstrated that by using such a mix a better registration can be obtained than by using points or surfaces alone.

Volume-Based Systems

Although volume-based registration has proven to be the best of the retrospective image-to-image methodologies (120), volumetric registration for image-guided therapy has proceeded slowly. The issue here is that if a high-quality intraoperative volumetric data set can be acquired, why use preoperative data at all? In certain specialized applications, such as therapy for prostate cancer, three-dimensional intraprocedural ultrasound can be matched to preoperative tomographic data on which therapy preplanning has occurred (121).

APPLICATION EXAMPLES

As stated at the beginning of this article, IGPs grew out of stereotaxy, driven by both the functional importance of tissue surrounding the site of surgical interest and the presence of the skull, which serves as a static mechanical platform for the soft-tissue target: the brain. However, IGPs were not merely improved stereotaxy, they opened the way for new modes of thinking about therapy delivery. The importance of specificity, of treating the lesion completely with as little damage to healthy collateral tissue as possible, came to the forefront. With the parallel development of minimally invasive techniques in other fields, we are beginning to see a convergence, with IGP being used for abdominal, spinal, and other forms of therapy.

Intracranial Resection/Ablation

Given the preponderance of intracranial neurosurgery and otolargyngological applications described earlier, it would take an article much bigger than this to cover the clinical applications of IGP in the head [for more complete references see (122–125)]. However, it is here, where the field is most mature, that the results of the first generation of work and ideas for the second generation can be seen. For cancer cases, the ultimate assessment is, do the patients have better outcomes with IGP than with previous methods. Perhaps the best data for that comes from the work done by Berger and coworkers (126, 127). In their papers, significantly better outcomes are demonstrated using resections to imaging defined margins as opposed to visually defined margins.

In addition, the presumption that tissue is rigid has been discarded, and mechanisms for correcting for periprocedural tissue deformation are coming on line. These include biomechanical models of the tissue (112, 128, 129) and the use of intraoperative ultrasound imaging to gather information for the correction of preoperative, high signal-to-noise images (130, 131).

In emerging image-guidance systems, we are beginning to see functional mapping play a greater role than in first-generation systems, in which all guidance has been done by anatomic image sets. The functional information is coming from position emissions tomography, functional MRI, and “superbrain” image sets in which a functional atlas is defined. In the case of the atlas, it is nonrigidly registered to the patient’s image set. The resulting deformations can then be applied to the functional data, providing a probabilistic functional map of the patient. It is in the placement of deep brain stimulators that this work has shown the most growth.

Beyond purely surgical intervention, IGPs have been used to place controlled-release chemotherapy agents in brain tumors (132), and there has been discussion of using these techniques for placement of gene therapy agents to improve their efficiency (133).

Although cancer therapies have dominated the intracranial applications, IGPs have had a role in vascular surgeries (134, 135), and image-guided radiosurgeries for vascular abnormalities have become commonplace (136, 137).

Functional Neurosurgery and Stimulator Placement

The use of electrophysiological data for guidance goes back to the beginning of stereotaxy. Interventional applications, such as ablations of foci of abnormal electrical activity for interruption of epileptic seizure initiation or propagation (138, 139) and ablations of deep gray nuclei for alleviation of Parkinson’s disease tremors (140, 141), used imaging to approximate the ablation site but used electrophysiological recording for final guidance. Additionally, ablations have been performed for the relief of chronic, previously intractable pain, such as that arising from some forms of cancer (142, 143). However, such techniques were limited by the variability of anatomy, distribution of function, and presence of space-occupying lesions. However, two recent developments are spurring additional growth. The first is the use of implantable stimulators to act as reversible ablations (144, 145). This means that cellular disruption need not be a permanent step. The second advance is the use of image volumes as atlases to allow the better integration of data across patients (146, 147). In addition, the use of functional MRI as a data source for IGPs promises to provide patient-specific functional information. However, continued work is needed to fully understand the fMRI images and to validate their use. Beyond surgical ablation and the placement of stimulators, image-guided radiosurgery (148) has found applications in functional procedures.

Spinal Applications

Over a quarter of a million lumbar spine operations will be done in the United States this year. The federally funded Back-Pain Patient Outcomes Assessment Team (HS 06344) placed the cost of back pain, the leading cause of loss of work days in the United States, at $50 billion. Beyond the lumber problems, cervical spine fractures and cystic, vascular, and neoplastic diseases of the spinal cord add a significant number of cases each year. The nature of the spine represents a substantial challenge for image-guided techniques. The spine cannot be presumed to be monolithically rigid; rather, it is piece-wise rigid, with deformable structures between the rigid segments. This requires a system in which multiple registrations can be performed. Beyond the vertebral and disk structures, the spine is a web of ligaments and tendons with intertwined vascular structures and functionally vital nerve roots. The challenge is so complex that a workshop was held in 1999 to try to clarify the technical requirements for image-guided spine procedures (149).

One of the leading sources of failure in surgery to alleviate pain or structural failure is the change in the length and mechanics of the spine following surgical intervention. A recent advance in the use of struts, called spinal instrumentation, is replacing direct vertebral fusion. Often, to rigidly attach the instrumentation, the device is fixed to the vertebrae via the use of screws driven into the pedicle of the vertebrae. Because the spinal cord, nerve roots, and supporting vasculature all lie within millimeters of the pedicle, accurate guidance is essential. Image-guidance techniques using preoperative tomograms and intraoperative imaging such as dual fluoroscopy have been developed (150, 151).

Although tumors of the spine represent a lesser health care issue than does back pain or trauma, the occurrence is devastating to the individual. IGPS both surgical (152, 153) and radiosurgical (154) are showing promise for more specific resection.

Orthopedics

Although neurosurgical applications were driven by the functional importance of intervening tissue between the skull and the lesion, orthopedic applications were driven by the need for accurate and precise control of position and angle. It is the need for precise positioning of position and angle that opens the doors for robotic IGPs. Although robots have been used in surgery for a while (155, 156), their role has been essentially device holder. The Robodoc system (157, 158), with an active head, is essentially an image-guided, numerically controlled milling machine. This allows the very accurate and precise placement of artificial hip components both in the femur and on the pelvis. Beyond hip replacement procedures, additional orthopedic applications include use in acetabulature fractures (159) and in osteotomies (160).

Abdominal

As IGPs prove their worth in intracranial, spinal, and orthopedic applications, their potential value in abdominal surgeries becomes more apparent. Two of the early targeted areas have been the liver and the prostate. In both, the major challenge is registration. Unlike the skull, the vertebrae, or the long bones, in liver and prostate there can be no presumption of even piece-wise rigidity.

In liver surgery, intraoperative ultrasound has become the standard for image guidance (161, 162). However, ultrasound is a low signal-to-noise imaging modality, and it is difficult to localize the center of a three-dimensional target. Recent work (163, 164) is bringing three-dimensional localization and guidance into liver surgery. Additionally, image-guided cryosurgery (ablation of tissue with extreme cold) (165) and interstitial photon radiation therapy (166) have been applied to the liver.

Prostate cancer is one of the most commonly occurring forms of cancer, and new blood chemistry studies have increased the detection rate of that cancer. However, optimum treatment remains difficult. Transperineal approaches have been developed, but patient posture and bladder fullness can cause significant changes in prostate position and orientation. Intraprocedural imaging, such as transrectal ultrasound (167–169) and intraprocedural MRI (170), have helped improve guidance. Interstitial brachytherapy (169, 171) has been shown to be effective and relatively safe. However, techniques need to be developed to correct for changes in the prostate during brachytherapy seed placement (172) and for deflection of the radioactive seed placement needle.

CONCLUSIONS

Although there has been an explosion of interest in image-guided procedures (IGPs) over the past decade, and a single review article is defined as much by what it leaves out as what it contains, we are still very much in the first generation of

IGPs. For the most part, we deal with tissue as if it is monolithic and rigid, we guide procedures based on anatomy rather than function, and we are crudely integrating image information over time and space. The biggest question, do IGPs produce better outcomes, is only now being addressed. However, there are some signs that we can point to. Once implemented on a regular basis, IGPs take less operating room time than do equivalent stereotactic procedures (173), IGPs are rapidly being integrated with minimally invasive procedures to reduce patient discomfort and recovery time (174), and IGPs are enabling technologies, allowing the possibility of successful treatment where it was not possible before.

Having demonstrated that IGPs can be made to work and having some evidence that they have positive clinical outcomes, considerable effort needs to be placed into validation and assessment of systems and techniques. One of the difficulties in comparing published results of IGPs is that system performance is not measured in a consistent manner. For example, some users of localizers report precision where some report accuracy. There is, as yet, no satisfactory way to assess the accuracy of a surface-based registration using only the two sets of surface points. The field needs independent assessment measures perhaps developed through the National Institute for Standards and Technology. If these tests can be developed and agreed on, then when a new technology or process emerges, it can be assessed on a level playing field.

The maturation of IGPs requires a change in research teams as well. Any system where the design engineer presumes to understand a proceduristʼs needs and builds a device to those standards is doomed to failure. Correspondingly, the field has demonstrated that a successful device or process requires a level of technical sophistication beyond that of physicians working on it in their spare time. Successful creation, development, and refinement and appropriate testing of IGPs is going to require teams of physicians, engineers, computer scientists, nurses, and clinical trial and outcome experts. However, the potential payoff is enormous. By guiding therapy to where it is needed, and by avoiding healthy structures, both the process and the outcome are improved.

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