Assessment of Hepatic Motion Secondary to Respiration for Computer Assisted Interventions

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ABSTRACT

This article reviews the published efforts to characterize hepatic motion secondary to respiration, with the specific goal of defining the limitations and potential applications of image-guided systems in percutaneous liver interventions (computer assisted interventions). Hepatic motion and deformation due to respiration remain obstacles to applying stereotactic localization techniques to the liver. Respiratory-associated hepatic motion is complex. Nine studies using diagnostic imaging or modeling are reviewed, and their findings are tabulated herein. The significant variations in their findings are discussed, including cranio-caudal translation, anterior–posterior and lateral translation, movement secondary to tissue deformation, and motion with respect to surrounding tissue. Techniques for correcting for hepatic respiratory motion are then described, including gating techniques, modeling approaches, real-time liver tracking, and magnetic tracking technology.

INTRODUCTION

Percutaneous minimally invasive procedures offer significant advantages over traditional surgical alternatives, including lower significant complication rates, shortened hospital stays due to decreased recovery time, and decreased expense.1 The liver is a frequent subject for a variety of medical interventions, and a rich assortment of percutaneous hepatic procedures has been developed. These procedures include percutaneous or endoscopic biliary drainage and cholecystostomy, percutaneous or transjugular needle biopsy, transjugular intrahepatic portosystemic shunt creation (TIPS), chemooembolization, and, more recently, percutaneous radiofrequency ablation. Hepatocellular carcinoma, for example, can be successfully treated with percutaneous ablation in the case of inoperable tumors, or as an adjunct prior to surgical resection.2,3

Hepatic motion secondary to respiration is a significant obstacle to precise percutaneous needle or instrument placement. Real-time ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI), while useful for inter-
vventional guidance, have significant drawbacks that prevent them from becoming complete solutions for procedural guidance. CT fluoroscopy is becoming more popular, although the potentially increased radiation dose to the patient and operator may limit the application of this technology. The application of computer-assisted surgery, including frameless stereotaxy and image guidance, may enhance the degree of precision obtainable by overcoming some of the limitations inherent in US, CT, and MRI. The purpose of this article is to summarize the reported characteristics of hepatic respiratory motion and deformation. Approaches to quantifying and correcting for this movement will be considered with the intention of providing a framework for further development and application of hepatic computer assisted surgery in patient care.

PERCUTANEOUS APPROACHES TO THE LIVER

Applications, Requirements, and Obstacles

Computer-assisted, image-guided approaches to diagnosis and treatment of liver disorders are already widely used with success. Current image-guided hepatic diagnostic procedures include percutaneous biopsy of intrahepatic masses presumed to be tumors, and internal/external biliary drainage for benign and malignant biliary duct obstruction. Additionally, conventional hepatic arteriography is performed both for diagnostic purposes, including hepatic transplantation evaluation, and for therapeutic goals, such as in hepatic trauma management.

Current percutaneous therapeutic applications include tumor ablation, cryotherapy and brachy-therapy, tumor embolization, and delivery of gene therapy vectors. Percutaneous procedures in the liver typically require a relatively high degree of accuracy, although this has not been definitively quantified. Accuracy may have different significance for individual applications. For example, in ablative procedures, placement of the radiofrequency or cryoprobe in the tumor center must be achieved with consideration of the exact zone of ablation relative to tumor margins and adjacent vital structures. In biopsy procedures, accurate needle placement at the tumor margin, rather than in the necrotic center, increases the diagnostic yield. Finally, accurate percutaneous needle placement in intrahepatic biliary ducts typically requires an accuracy of several millimeters over the needle trajectory course of several centimeters. Accuracy requirements will expand as targets for therapy such as micrometastases become smaller—a current trend in cancer treatment and gene therapy. However, achieving the required precision in minimally invasive procedures is complicated for moveable, deformable organs such as the liver.

A more precise definition of accuracy will be required in the future for these novel therapeutic procedures, including ablations, antiangiogenesis, and gene therapy. Current non-real-time guidance modalities such as CT will be inadequate, while real-time modalities such as US typically require considerable operator skill and coordination, potentially limiting the availability of new interventions. There is, therefore, potentially a significant role for a non-real-time, image-based guidance system that does not employ ionizing radiation.

US offers the distinct advantage of real-time imaging capability without using ionizing radiation. It is, however, an inherently noncoordinate technology that does not lend itself to stereotactic localization of tissue. Although US does provide a visual display of the operative field, it is limited to a two-dimensional display in most common applications. Even in the form of three-dimensional (3D) US, it cannot convey the precise coordinate location of tissue and instruments that is required to achieve high levels of precision. Stereotactic image-guided systems based on US, such as UltraGuide, have been introduced, but are not yet in widespread use and have other technical limitations related to needle bending. Other weaknesses of US include high interoperator variability, inability to penetrate gas-filled overlying colon, limited resolving power, and the image obliteration that occurs after an ablative procedure.

The use of MRI, either as an adjunct to or a replacement for US, has been explored as a possible remedy for these limitations. Static MRI and CT images are routinely used for preoperative planning. Both CT and MRI provide excellent visualization of target-tissue detail. Concurrent CT or MRI images help identify suitable approaches to the intended target. However, successful needle or instrument placement under CT/MRI image guidance is a repetitive needle-repositioning exercise. The needle is gradually advanced and/or redirected while its position is reassessed with a new static image until the desired needle position is obtained. The primary disadvantages of this process of “advance and check” are the additional time required for reimaging and the accuracy limitations introduced by respiratory or patient motion. Needle
placement for interventions also requires a high degree of operator skill.\textsuperscript{17} CT fluoroscopy is a recently introduced imaging modality that combines the anatomic resolution of CT with the real-time imaging capabilities of fluoroscopy. One drawback is that CT fluoroscopic imaging may expose both the patient and the interventionalist to increased doses of ionizing radiation.\textsuperscript{18,19}

Regardless of the imaging modality employed, percutaneous interventions in the liver using this advance-and-check technique for needle or instrument placement share complication risks. The risk increases with the number of needle passes undertaken. Hemobilia, intraperitoneal hemorrhage, and hemothorax have been reported.\textsuperscript{2} Complications also include bile-duct injury,\textsuperscript{20,21} and seeding of the needle tract with tumor in ablative procedures.\textsuperscript{21–24} The ideal method of intraoperative guidance would provide precise path planning, tissue visualization, and real-time guidance as aids to a single successful puncture effort. Successful interventions could therefore be potentially completed with a substantially reduced complication rate.

### Frameless Stereotactic Guidance

The possibility of extending the technique of frameless stereotaxy to the liver is fairly novel, but has been explored by Herline et al.\textsuperscript{13,15} Frameless stereotactic instrument guidance has been very successful in brain and spine interventions.\textsuperscript{25} Discussions of the required degree of accuracy typically state the needed margin to be 5 mm.\textsuperscript{26} In addition, frameless stereotactic neurosurgery has reduced interoperator variability and decreased ancillary trauma by eliminating the need for multiple needle passes.

Liver motion secondary to respiration remains a substantial barrier to implementing frameless stereotaxy for hepatic applications. The stereotactic techniques developed for neurosurgical applications use preoperatively acquired CT or MRI images, which are mapped to the surgical field using image registration. During the procedure, the position of the instruments and tissues can be displayed and updated on the reference images in real time. This requires that the target tissue remain motionless for the registered image to be valid for instrument guidance.\textsuperscript{25} Unfortunately, the liver does not meet this requirement.

### Assessments of Hepatic Respiratory Motion: Review

Adequate characterization of hepatic motion due to respiration is an essential first step in the development of computer-assisted surgical guidance systems.\textsuperscript{13} This understanding is necessary to determine the motion parameters of these systems and to select the optimal portion of the respiratory cycle for manipulating instruments. However, only limited quantitative information is available to date.\textsuperscript{27} To identify appropriate studies for this review, the National Library of Medicine’s PubMed database was searched using the search terms: “liver motion,” “hepatic motion,” and “respiration.” Appropriate conjunctive and disjunctive modifiers were used to narrow the search, and relevant studies, including those that measured liver or diaphragmatic motion, were reviewed. Earlier studies cited in these works, but not found in Medline, were identified and assessed. The body of literature assessing hepatic respiratory motion is not large. Therefore, all of the identified studies that quantified liver motion are discussed herein.

Of the existing reports, several describe efforts to reduce image artifacts generated by organ motion or to improve the targeting of neoplasms for radiotherapy.\textsuperscript{28–31} Other studies of liver motion used scintigraphy,\textsuperscript{32,33} US,\textsuperscript{27,34} CT,\textsuperscript{34} or MRI\textsuperscript{15} for measurement. One study additionally reported maximum respiratory-related hepatic velocity and acceleration.\textsuperscript{27} Other reports focus on tracking the movement of the center of an isolated spherical liver tumor during the respiratory cycle using high-speed MRI.\textsuperscript{36,37} Finally, another group employed the registration of serial MRI images to evaluate the motion and deformation of the liver.\textsuperscript{38}

Although new ultrafast CT and shortened MRI image-acquisition times have made it possible to reduce the impact of liver motion on image acquisition, hepatic respiratory motion continues to be critical in radiotherapy for liver cancers.\textsuperscript{39} Researchers have focused on ways to compensate for tumor motion so that as much normal parenchyma as possible can be spared. Recently, one group has assessed hepatic motion secondary to respiration in both human subjects and a porcine model specifically to assist in the development of a frameless stereotactic surgical system.\textsuperscript{13}

Considered together, these reports show liver movement to be complex, with cranio-caudal, lateral, and anterior–posterior motion, in addition to movement due to deformation of the tissue. They
also demonstrate that there is wide variation between individuals in the degree and direction of liver movement. Table 1 summarizes the results of nine published studies of hepatic motion in human subjects.

### Cranio-Caudal Translation

As indicated in Table 1, all studies agree that cranio-caudal motion is the most significant, with translation ranging from 10 to 26 mm in quiet respiration. The MRI study by Korin et al. suggested that clinically significant liver motion could be approximated effectively by cranio-caudal movement alone, completely neglecting other axes of motion. This conclusion was sustained by the US studies of Davies et al. the following year. Although this approximation would simplify the modeling and tracking of hepatic motion, more recent studies suggest that translations along the other axes, as well as motion due to deformation, are significant and cannot be neglected.

### Anterior–Posterior and Lateral Translation

Measurements of movement in both the anterior–posterior (AP) and lateral directions vary markedly with the assessment technique used, and there has been disagreement in the literature about the significance of these components of motion. Davies et al. and Korin et al. initially reported minimal motion in both the medial–lateral and AP directions. The more recent evaluations by Herline et al. (using optical tracking), Shimizu et al., and Rohlfling et al. (both by MRI), however, indicate that there is significant translation along both of these other axes. Shimizu et al. observed solid tumor movement within the liver throughout the respiratory cycle and reported average movement of 8 mm AP and 9 mm lateral, with similar results in a follow-up study. Rohlfling et al., in their analysis of liver motion in a single patient by serial registration of MRI images, also reported significant movement in the AP and lateral directions, as shown in Table 1. This difference between early and later evaluations in the reported significance of liver motion perpendicular to the cranio-caudal plane is due to differences in detection techniques and standards for evaluation. Korin et al. and Davies et al. evaluated the motion of liver margins in MRI and US images. The later studies followed the motion of single (in the case of tumor tracking) or multiple points within the liver volume. This distinction is significant, because measurement of movement about hepatic margins would intrinsically underestimate motion due to deformation inherent in a nonrigid tissue such as the liver. In addition, tracking of points within the liver volume yields results more directly relevant to the goal of tracking intrahepatic targets for interventional guidance. Based on these considerations, it is clear that lateral and AP translation is significant, particularly when tracking discrete targets within liver tissue.

### Movement Secondary to Tissue Deformation

The liver is a nonrigid organ with a thin, flexible capsule that does not prevent deformation. Korin et al. determined that the deformation of the liver during the respiratory cycle appeared to be insignificant according to their MRI line-scan technique, estimating deformation to be less than 3 mm. However, the analysis by Rohlfling et al. of hepatic motion by intensity-based free-form deformation registration found significant movement due to

### Table 1. Hepatic Motion Secondary to Respiration in Nine Human Studies

<table>
<thead>
<tr>
<th>Study/date</th>
<th>Number of subjects</th>
<th>Quiet inspiration</th>
<th>Deep inspiration</th>
<th>Anterior-posterior (mm)</th>
<th>Lateral (mm)</th>
<th>Modality</th>
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<tr>
<td>Weiss (1972)</td>
<td>12</td>
<td>11 ± 3</td>
<td>12–75</td>
<td></td>
<td></td>
<td>Scintigraphy</td>
</tr>
<tr>
<td>(using scintigraphy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(using fluoroscopy)</td>
<td>25</td>
<td>13 ± 5</td>
<td></td>
<td></td>
<td></td>
<td>Fluoroscopy</td>
</tr>
<tr>
<td>Harauz (1979)</td>
<td>51</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td>Scintigraphy</td>
</tr>
<tr>
<td>Korin (1992)</td>
<td>15</td>
<td>13</td>
<td>39</td>
<td>2.5</td>
<td></td>
<td>MRI</td>
</tr>
<tr>
<td>Davies (1994)</td>
<td>9</td>
<td>10 ± 8</td>
<td>37 ± 8</td>
<td></td>
<td></td>
<td>US</td>
</tr>
<tr>
<td>Herline (1999)</td>
<td>2</td>
<td>10.8 ± 2.5</td>
<td></td>
<td></td>
<td></td>
<td>Optical tracking</td>
</tr>
<tr>
<td>Shimizu (1999)</td>
<td>1</td>
<td>21</td>
<td></td>
<td>8</td>
<td>9</td>
<td>MRI</td>
</tr>
<tr>
<td>Shimizu (2000)</td>
<td>6</td>
<td>10.6 ± 7.0</td>
<td></td>
<td>4.6 ± 1.6</td>
<td>5.2 ± 1.8</td>
<td>MRI</td>
</tr>
<tr>
<td>Rohlfling (2001)</td>
<td>4</td>
<td>12–26</td>
<td></td>
<td>1–12</td>
<td>1–3</td>
<td>MRI</td>
</tr>
</tbody>
</table>
deformation. Because the liver is nonregular in shape and somewhat nonuniform in composition (due to the location of vascular structures and ligamentous tissue), the degree of deformation varies markedly within the organ. The registration technique used by Rohlfling et al. is a particularly sensitive way to evaluate point-by-point changes in location throughout the respiratory cycle, and to compare rigid assumptions of movement with the changes that actually occur. This group reported that tissue deformation of the liver with respiration is substantial. When point-by-point measurements of locations within the liver were tracked throughout the respiratory cycle, they differed from the predictions made by models that assumed rigid motion by between 2 and 19 mm, with an average of 6 mm across the tissue. Mis-registration was found to be most pronounced at the superior and inferior margins of the liver. Other researchers estimated the error introduced by assuming rigid liver motion to be 3 mm on average. 

**Motion with Respect to Surrounding Tissue**

The liver does not have a fixed relationship to the skin surface or surrounding organs during the respiratory cycle, further complicating motion characterization. Two investigators addressed this issue in an attempt to evaluate respiratory gating protocols, which assume that the liver recovers the same position at identical moments in the respiratory cycle. Suramo et al. determined that the liver attains the same position in only 18% of gated CT and US exposures. Twenty percent of views yielded “markedly different” liver positions (outside the CT slice, or greater than 4 mm displacement), despite identical timing of exposure by a form of respiratory gating. This group concluded that any procedure that cannot be completed within one breath-hold would be affected by this inaccuracy. Shimizu et al. evaluated the position of hepatic tumors with respect to the overlying skin surface for possible radiotherapy treatment volume reduction by respiratory gating. They reported that the position of the tumor contours was not constant with respect to the skin surface at peak exhalation or inhalation in each respiratory cycle. This finding contradicts the previous assumption in respiration-gated radiotherapy that the position of the tumor is constant at the exhalation peak.

**CORRECTION FOR HEPATIC RESPIRATORY MOTION**

The liver moves during inspiration and surgical manipulation, and when the patient changes position to any degree. Suramo et al. described the liver as the “most moveable (abdominal) organ in both normal respiration and standardized breathing.” It seems clear from the literature that hepatic motion consists of translation along every axis as well as movement due to deformation of the tissue itself. Accurate targeting of the moving liver therefore requires a system that can correct or account for a very complex range of movement.

Frameless stereotactic guidance for moving organs requires that the target be tracked and registered with preoperatively acquired images. This can be accomplished in several ways. Breath-holding and gating techniques attempt to time specific procedures to coincide with a fixed point in the respiratory cycle when the liver is assumed to be motionless and therefore in registration with the preoperative images. Modeling techniques track the motion of the liver over several cycles, and then construct a predictive model of motion based on this information. Other strategies track the liver in real time, updating the guidance information with the current organ position. Several variations on these approaches have been reported in the literature as described below.

**Gating Techniques**

“Respiratory gating” is an approach that permits the approximation of a motionless liver by operating on the tissue intermittently only at identical points in the respiratory cycle. It is even possible to register the tissue to preoperative images also taken at the specified lung volume. End-exhalation is the point most often chosen, because it represents the longest natural pause in the cycle. Gating techniques to compensate for liver motion have been used in radiotherapy and artifact correction in MRI and CT images with some success. Tissue motion gating for radiotherapy can potentially deliver an optimal radiation dose to the tumor while minimizing exposure of adjacent healthy tissue. 

Respiratory gating techniques for surgical guidance require that identical moments in successive respiratory cycles can be isolated to serve as a “trigger” for image acquisition and 3D space registration. A mass, biliary duct, or hepatic vessel could then be consistently targeted for intervention. This assumes that the liver reoccupies the same position at equivalent moments within the cycle. However, measures of hepatic respiratory motion indicate that the liver does not reliably assume the same position at equivalent lung volumes or identical moments in the respiratory cycle.
sult, “breath-hold” and gating techniques may be inadequate for precise guidance of hepatic interventions without real-time imaging assistance.

Modeling Approaches
Modeling of liver motion to predict the location of a target from previously acquired images is another approach that has been explored. However, if the movement varies between cycles, prediction of that variability with sufficient precision represents an unsolved technical problem. Modeling cannot, therefore, provide sufficient precision for prospective use, although it has been used retrospectively for motion correction with some success.38

Real-Time Liver Tracking
Real-time liver tracking strategies for procedure guidance obviate the requirement for a motionless liver by using computer correction. This strategy tracks the target tissue within the liver along with the surgical instruments, updating these positions in real time on guidance images. Herline et al. used a combined surface and point-based registration technique to register preoperative images to intraoperative liver motion in human subjects to quantify hepatic movement (see Table 1). They then expanded upon that work by using this image-registration technique for stereotactic guidance in a porcine model.15 In this study, a digitized liver surface, along with discrete surface and internal liver points (e.g., edge of the falciform ligament, portal vein bifurcation) were used in the registration. Tracking was provided by an Optotrak (Northern Digital Inc., Ontario, Canada) optical tracking system. The reported error using this combined technique was 2.9 mm for the entire surface and 2.8 mm for embedded targets. This work shows that stereotactic tracking of a moving liver is feasible with a high degree of accuracy during open surgical procedures. However, obtaining this degree of accuracy without surgically exposing the liver for surface registration still needs to be investigated for minimally invasive approaches. It is also important to stress that, although this assessment of liver motion was consistent with values reported in other studies, Herline et al. used measurements obtained in an open surgical setting.

Schweikard et al. investigated methods to compensate for hepatic tumor motion secondary to respiration for robotic radiosurgery.39 The achievement of the desired surgical margins during radiosurgery often results in a higher-than-desired radiation dose to adjacent normal tissues. Schweikard et al. were able to track the motion of a hepatic tumor and use this information to guide a robotically controlled therapeutic source, thereby reducing the treated tissue volume, as well as the damage to normal tissue. They determined the location of the moving tumor by combining optical tracking of the patient’s skin with synchronized X-ray imaging of internal markers, which were continuously updated during treatment to provide motion compensation. This technique provides an example of real-time liver tracking achieved without surgical liver exposure. The same technique could potentially be implemented for other minimally invasive interventions in the liver and other deformable organs.

Magnetic Tracking Technology
Magnetic tracking technology has been previously employed for real-time intra-abdominal organ tracking without surgical exposure. Solomon et al. demonstrated the feasibility of at least three percutaneous interventional procedures using real-time magnetic tracking registered with cross-sectional images.41–43 They performed a transjugular intrahepatic portosystemic shunt (TIPS), transbronchial needle aspiration in swine, and placement of an inferior vena cava filter using this technology. Other investigators used magnetic tracking in electro-anatomical mapping of the heart, thereby obviating the need for fluoroscopy.44 These examples demonstrate the versatility and applicability of this integrated technology in multiple organ systems. In the TIPS procedure performed by Solomon et al., the actual position of the needle instrument was registered with preoperative images, allowing the operator to successfully puncture the portal vein in transhepatic fashion without visualizing the target with a real-time imaging modality.41

Our own research group at Georgetown has been developing a percutaneous needle placement paradigm using magnetic tracking of the respiratory-related motion of the liver registered with preoperatively acquired CT images.45 We therefore developed a liver respiratory motion simulator to test the feasibility of direct percutaneous puncture of an intrahepatic vessel whose position during the respiratory cycle is extrapolated from the position of an intravascular fiducial within the liver.46 Banovac et al. demonstrated the anatomic feasibility of percutaneous anterior transhepatic simultaneous portal-hepatic vein punctures by retrospective image analysis.47 This serves as a basis for further work in this new approach to the TIPS procedure.

Using active liver motion tracking based on the AURORA™ magnetic localization system (Northern Digital, Inc., Ontario, Canada) and a
small percutaneously placed needle fiducial, the feasibility of transhepatic portal-hepatic vein puncture has been shown. With magnetic tracking assistance and a new needle-placement algorithm, this approach may be simpler to perform than the traditional transjugular approach. Additionally, the accuracy of percutaneous needle placement for purposes of liver lesion biopsy or thermal ablation has also been demonstrated in a respiring liver phantom. Although animal and human studies must be undertaken to confirm this early work, magnetic tracking appears promising as a modality for liver localization and tracking. Moreover, magnetic tracking may improve organ localization in general and lead to development of new surgical navigation methods for procedures involving other internal organs.

CONCLUSION

Nine published studies of respiratory-associated hepatic motion were reviewed with the goal of defining the limitations and potential applications of image-guided systems in percutaneous liver interventions. The significant variation in these studies has been discussed, and techniques for correcting for hepatic respiratory motion have been described.

However, in current clinical practice, catheter- and needle-based interventions in the liver are already performed with a high degree of success and relatively low complication rates. Therefore, what improvement in outcome can be expected from the use of frameless stereotaxy in minimally invasive hepatic interventions?

First, magnetic tracking may play a significant role as an adjunct guidance system for percutaneous intrahepatic procedures where traditional real-time imaging guidance is not feasible, for example, where lack of an adequate acoustical window precludes adequate US imaging, or where patients cannot cooperate with respiratory instructions for “breath-hold” approaches. The technical feasibility and radiation doses absorbed by patients and operators with CT fluoroscopy must be elucidated before this technology becomes widespread. Second, magnetic guidance may help improve the skills of practitioners who otherwise would have limited experience performing these procedures. Third, with the aid of magnetic tracking systems, experienced practitioners may enjoy shorter procedure times, thus reducing hospital costs and associated morbidity. Finally, the possibilities exist for the future integration of this technology with gene delivery, antineoplastic, or antiangiogenesis therapies.

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