Toward Integrated Image Guided Liver Surgery

W. R. Jarnagin[a*], Amber L. Simpson[a], and M. I. Miga[b,c,d,e,**]
[a]Hepatopancreatobiliary Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
[b]Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA
[c]Department of Radiology and Radiological Sciences, Vanderbilt University Medical Center, Nashville, TN, USA
[d]Department of Neurological Surgery, Vanderbilt University Medical Center, Nashville, TN, USA
[e]Vanderbilt Institute in Surgery and Engineering, Vanderbilt University, Nashville, TN, USA

ABSTRACT

While clinical neurosurgery has benefited from the advent of frameless image guidance for over three decades, the translation of image guided technologies to abdominal surgery, and more specifically liver resection, has been far more limited. Fundamentally, the workflow, complexity, and presentation have confounded development. With the first real efforts in translation beginning at the turn of the millennia, the work in developing novel augmented technologies to enhance screening, planning, and surgery has come to realization for the field. In this paper, we will review several examples from our own work that demonstrate the impact of image-guided procedure methods in eight clinical studies that speak to: (1) the accuracy in planning for liver resection, (2) enhanced surgical planning with portal vein embolization impact, (3) linking splenic volume changes to post-hepatectomy complications, (4) enhanced intraoperative localization in surgically occult lesions, (5) validation of deformation correction, and a (6) a novel blinded study focused at the value of deformation correction. All six of these studies were achieved in human systems and show the potential impact image guided methodologies could make on liver tissue resection procedures.

Keywords: Image Guided Surgery, Registration, Liver, Resection, Finite Elements, Models

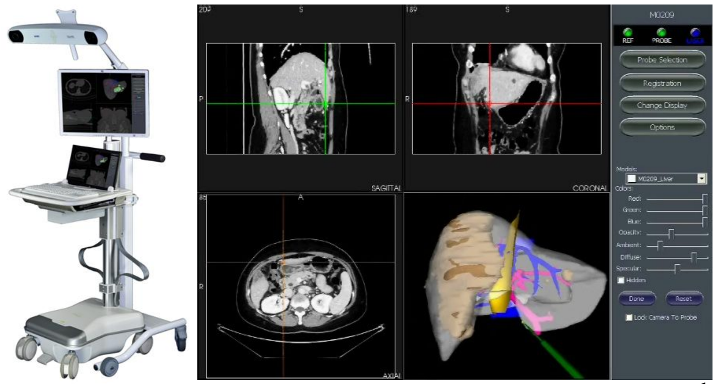
1. INTRODUCTION

1.1 Future Opportunities in Liver Resection Procedures

Resection of liver tumors remains a specialized and highly complex procedure that requires consideration of many variables (e.g. vascular control, distribution of tumors, and adequate residual liver volume). Previously a risky and resource-intensive procedure, hepatic resection is now commonly performed for an increasing number of indications. The excellent five year survival rate (e.g. 44-50% with metastatic colorectal tumors [3]) make it the gold standard approach [4] to treating selected patients with primary and metastatic liver cancer [5], despite its complexity. As the safety of the procedure has improved, the indications for hepatic resection have expanded to include patients with more advanced disease. In this regard, resection of multiple segments, resection combined with ablation, and two-stage resection are being performed with greater frequency. Interestingly, investigators are now using other treatments, usually systemic chemotherapy, not as curative measures but to facilitate surgical therapy, or even embolization techniques to increase healthy liver surgical remnant [6]. While aggressive surgery is very effective, we must acknowledge that it risks injury to the liver parenchyma, which can impair normal regeneration and put patients at risk for post-operative liver failure [7]. With this backdrop, realization of image-guided liver surgery (IGLS) should enhance resection, maintain parenchymal preservation and vascular control, enhance laparoscopic approaches, and extend to other therapeutics domains such as microwave ablation (still currently considered inferior to resection).

* jarnagiw@MSKCC.ORG, **Michael.I.Miga@vanderbilt.edu

Medical Imaging 2017: Image-Guided Procedures, Robotic Interventions, and Modeling, edited by Robert J. Webster III, Baowei Fei, Proc. of SPIE Vol. 10135, 101350R · © 2017 SPIE
CCC code: 1605-7422/17/$18 · doi: 10.1117/12.2257615



a b

Figure 1. (a) Explorer™ guidance system and (b) display. Reconstructed from [1].

1.2 Technology

The first FDA approved IGLS system in use in the US was created by Pathfinder Technologies, Inc. (Nashville, TN) and now supported by Analogic Corp. (Peabody, MA) and is shown in Figure 1. This system was developed through collaborative efforts between researchers at Vanderbilt University, Washington University, and Pathfinder Therapeutics Inc. The system was first evaluated by three independent clinical sites (University of Pittsburgh Medical Center, Memorial Sloan-Kettering Cancer Center, and University of Florida Medical Center). At this stage, the workflow associated with using the system in Figure 1a is similar to standard image-guided surgery platforms. Preoperative CT or MR patient images pulled directly from the Patient Archive and Communication System are used to create a surgical plan and then transferred to the intraoperative guidance platform. A rigid image-to-physical registration is performed and intraoperative assessment can move forward (Figure 1b). While somewhat standard, there are some very unique aspects to IGLS with the current platform. Specifically, the standard operating procedure is to acquire salient features (falciform, round ligament, and ridges) and the organ surface through optically tracked stylus swabbing. These data are used in an organ-to-organ registration which is quite different from the single-registration environment associated with image-guided neurosurgery (IGNS). This approach has been documented extensively in our own work [8]. While the platform itself is a step forward in innovation for liver surgery, the platform will also serve as the basis for our discussion and understanding the potential impact of image guided procedures on the abdominal environment in the future

2. EXEMPLAR STUDIES TOWARD REALIZATION OF IGLS

2.1 Accuracy of Surgical Planning

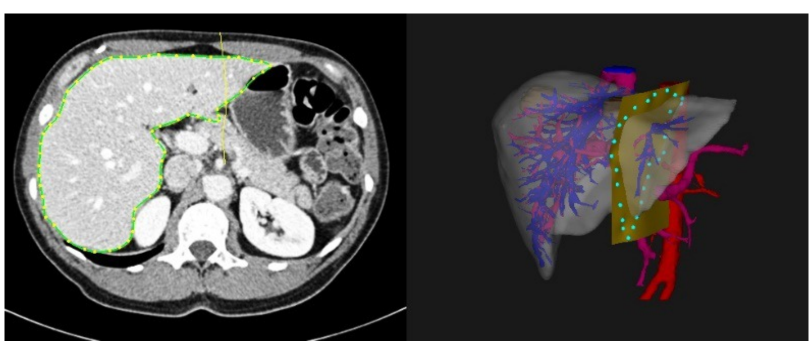


Figure 2. Sample data from Scout Liver planning software: (left) CT image with boundaries of organ indicated by green contour and (right) 3D model of organ with hepatic (red) and portal (blue) venous systems, tumor (brown), and resection plane. Reproduced from [2].

With respect to surgical planning, we studied the accuracy of our liver surgical planning software for predicting postoperative remnant liver volume (RLV) and assessing early regeneration [2]. Figure 2 is an example of our planning capabilities. Our surgical planning study involved sixty-six patients from three treatment centers and predicted that RLV correlated with actual RLV ($r=0.941$, $p<0.001$) as shown in Figure 3, which improved when timing of postoperative imaging was considered ($r=0.953$, $p<0.001$). Interestingly, when looking at relative volume deviation from predicted RLV to actual RLV and stratifying according to timing of postoperative imaging, the data showed evidence of measurable regeneration beginning five days after surgery, a new result in our understanding of liver regeneration ($p < 0.01$). These findings indicate that preoperative virtual planning of future liver remnant accurately predicts postoperative volume following hepatic resection. In addition, early postoperative liver regeneration is measureable on imaging beginning at five days following surgery. These findings are remarkable and reflect the use of surgical planning.

2.2 Increased Surgical Candidacy and Metastatic Disease Predictors

As discussed in the Introduction, treatment teams are always pursuing innovative ways to stratify patients to increase surgical candidacy while maintaining safe outcomes. In the course of our planning capabilities, we have made some strides towards the pre-hepatectomy strategy of portal vein embolization (PVE). PVE techniques have become an important approach to increase future liver remnant (FLR) before hepatectomy. However, measures in the post-PVE setting but prior to surgery have not been well developed for anticipating catastrophic conditions such as liver failure. In a retrospective study of 153 patients who underwent a major hepatectomy after PVE [6], we analyzed pre-post PVE MR or CT volumetric data using our planning software. The analysis showed poor predictive value of the more simplistic metric of post-PVE future liver remnant. However, measurements of the degree of hypertrophy and growth rate were

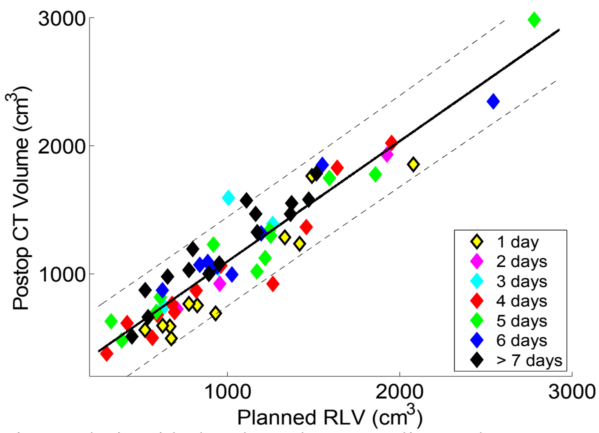


Figure 3. Scatterplot of the regression analysis with the planned remnant liver volume - RLV (virtual resection) and the actual RLV (postoperative CT volume) with the 95% confidence interval colored by the timing of the postoperative CT. There is good correlation between the planned RLV and postoperative volume. Note that the data points of earlier scans fall below the line and later scans above the line. Reproduced from [2].

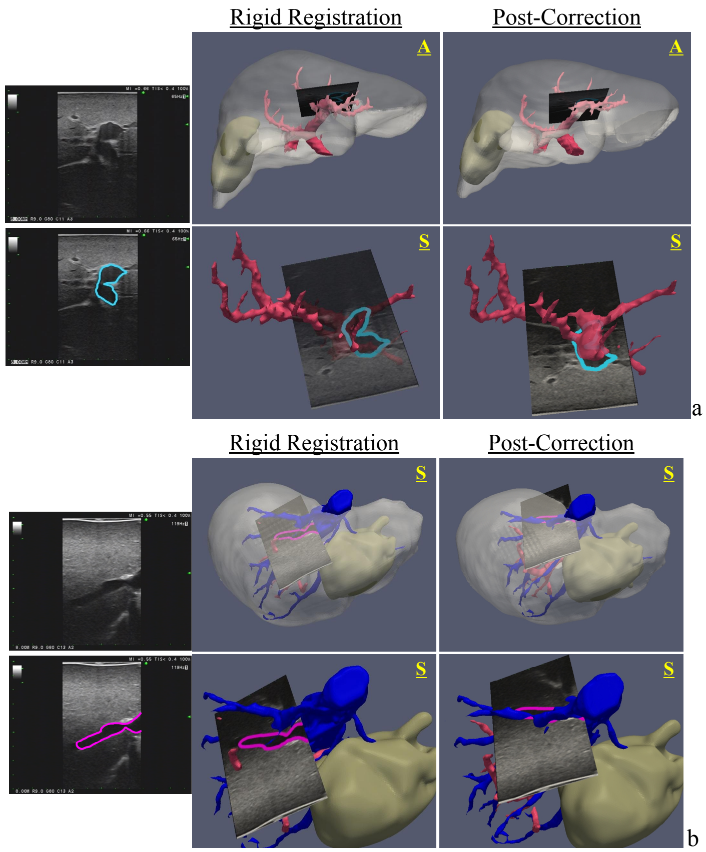


Figure 4. (a, b) Two sample cases showing misregistered subsurface features by rigid registration and improved alignment using nonrigid methods (compare white, and magenta arrow for each case.

good predictors of liver failure (area under the curve AUC=0.80; p=0.011 and AUC=0.79; p= 0.015, respectively) and modest predictors of major complications (AUC = 0.66; p=0.002 and AUC=0.61; p=0.032). Even thresholds were indicated; no patient with growth rate >2.66% per week had liver failure develop. In a third study, in [9], analyzing retrospective patient data with colorectal liver metastases, splenic volume changes showed to be an independent predictor of major post-hepatectomy complications, suggesting that the spleen is a 'thermometer' of metastatic disease. *It is interesting to consider, whereas surgical techniques and skill have been paramount in the past, work such as this begins to integrate data science and physiological strategies for improving surgical care.*

2.3 Enhancing Surgery Beyond with Radiographic Guidance

In [10], we investigated the use of the guidance system within the context of identifying small colorectal carcinoma metastases which often have poor ultrasound echogenicity from chemotherapy and other preoperative treatments. In a preliminary analysis of 18 patients, the guidance system found 60% of these occult lesions and changed intraoperative management of 17% of the cases. The full 50 patient trial recently concluded, demonstrating similar trends. A second 50 patient trial was recently approved which will investigate tumors that disappear in CT prior to surgery.

2.4 Quantitative Guidance Evaluation

While the above shows the value of planning and the potential surgical advancements that may be possible with the technology, it is important to assess the fidelity of the guidance system in a realistic setting. In a recent 6-patient study in [11], we utilized a novel nonrigid image-to-physical registration methodology we developed [12, 13] that uses sparse anterior liver surface data only to perform a full volumetric registration that accounts for rigid body rotations, and translations as well as accounts for soft-tissue deformations associated with organ presentation. In this study the methods were used to nonrigidly register preoperative image data to the intraoperative presentations using *sparse surface data only* acquired through optically tracked stylus swabbing (current standard for IGLS systems). In this study, tracked intraoperative ultrasound was employed as a means to identify subsurface vasculature and use them as *true targets to* *evaluate target error, i.e. ultrasound-identified vascular targets were NOT used in any way to drive the registration*. We were able to reduce target error of subsurface vascular targets from an initial error of 5.6 ± 2.2 mm to 2.7±0.7 mm following correction, an approximate 52% correction. Recent enhancements that support a more dynamic packing surface suggest we can improve on this. Figure 4 a,b demonstrates two results from [11]. In the first column of each is intraoperatively identified subsurface vascular targets via ultrasound. In the second column is the rigidly registered models of liver surface and vasculature derived from the preoperative CT images with tracked ultrasound target overlaid. Notice how the highlighted vascular components on the tracked intraoperative ultrasound do not line up with the

	Evaluation #					
	1	2	3	4	5	6
Rigid Registration	→	↓	↑	↓	↑	→
Enhanced Registration						
Surgeon Score	0	3	-3	3	-3	0

Table 1. Evaluation table (arrow indicates display transition for evaluation). Scores averages in (b) reflect evaluations in 3 different surgeries with two different surgeons.

geometric model components derived from CT. This is indicative of the misalignment associated with rigid salient feature registration. The last column represents our model-corrected. In both examples we see improved alignment of these vascular targets (teal and magenta contours). We should also note that we have recently enhanced our approaches to improve robustness and alignment by adding more constraints, enhanced sampling techniques, and the incorporation of more deformation modes. The results in Figure 4 a,b are highly encouraging for our organ-to-organ nonrigid registration approaches.

2.5 A Novel Blinded Study Framework Toward Cognition of Enhanced Registration Techniques Intraoperatively

In some respect, the study in Figure 4 represents the quantitative aspects to correction but does not address the considerable difficulty of OR workflow, visualization, and utilization of correction. The most straight-forward means of introducing deformation correction would be to apply deformation fields to the images themselves. Unfortunately, much of the fine feature can be lost in this process due to interpolation effects associated with working on low soft-tissue contrast in CT (the most common liver imaging modality). As a result, we have developed a novel local stylus transform which corrects for deformation but also maintains the pristine nature of the images. Briefly explained, one could choose to account for deformation by deforming the images using the deformation field associated with the fitting process in [12, 13], or one could choose to shift the stylus position, models and other instrumentation according to the non-rigid deformation field provided and not alter the images – our novel transform methods reflects the latter. One might think this is non-optimal (e.g. perhaps a chasing effect); but, in a pilot study that compared mean performance with our method of applying the deformation to the tool tip versus the conventional technique, the methods were statistically similar with respect to accuracy of localization ($p<0.05$) and amount of time ($p<0.05$) required for localization of a target [14].

One particularly attractive feature that the methodology affords us is the ability to conduct a truly blinded bystander study. More specifically, as the patient imaging record is identical in assessing our guidance displays with either rigid or deformation-corrected, the surgeon assessing can do so in a truly blinded fashion; i.e. there are no visual cues indicating whether the display is uncorrected versus corrected. In fact, the only means to assess the display value is by testing the localization via interrogating the organ and looking at the localization on the images via the cross-hair. Taking advantage of this feature, we have just recently concluded a 20-patient novel bystander trial that is currently under review. The current trial entails 7 or more displays being *assessed during surgery* in sequence with the surgeon being asked on a +3 to -3 scale whether the display he or she is currently evaluating is better or worse than the previous. Table 1 demonstrates an example intraoperative evaluation outcome. Each arrow represents a transition from one display to the other with scoring being asked to the surgeon immediately after interrogation. When looking across each display trial, when the surgeon is transitioning from rigid to enhanced registration, the average score was +1.53 +/- 1.60 (n=55); when transitioning from enhanced to rigid registration displays, the average score was -1.43 +/-1.67 (n=46), and when the displays were held the same, the average score was 0.08 +/-0.83 (n=24). Clinical scores where improvement correlated with expectation were statistically significant at $p = 0.01$ (defined as a rating > 1) and degradations correlated with expectations at $p = 0.03$ (defined as a rating < -1). These initial results are highly encouraging. We believe this study ushers in a new testing paradigm for the relevance of nonrigid registration methodologies for image-to-physical registration. In addition, we are unaware of anything comparable in the context of IGLS, or IGNS.

3. CONCLUSION

This review of our work demonstrates dramatic impact with respect to (1) preoperative staging, (2) planning for resection surgery, (3) the power of soft soft-tissue modeling for updating image-guided navigational systems, and (4) the considerable capability that image guided technology provides to abdominal surgery. While not widely adopted yet, recognition of the benefit to these approaches is beginning. On a general note, the outcome of advances such as the ones above will result in the next revolution in comprehensive soft-tissue image-guided surgery system.

REFERENCES

[1] C. W. Hammill, L. W. Clements, J. D. Stefansic, R. F. Wolf, P. D. Hansen, and D. A. Gerber, "Evaluation of a Minimally Invasive Image-Guided Surgery System for Hepatic Ablation Procedures," *Surgical Innovation,* vol. 21, pp. 419-426, Aug 2014.

[2] A. L. Simpson, D. A. Geller, A. W. Hemming, W. R. Jarnagin, L. W. Clements, M. I. D'Angelica*, et al.*, "Liver Planning Software Accurately Predicts Postoperative Liver Volume and Measures Early Regeneration," *Journal of the American College of Surgeons,* vol. 219, pp. 199-207, Aug 2014.

[3] R. P. DeMatteo, C. Palese, W. R. Jarnagin, and e. al., "Anatomic segmental hepatic resection is superior to wedge resection as an oncologic operation for colorectal liver metastates," *J. Gastrointest. Surg.,* vol. 4, pp. 178-184, 2000.

[4] K. Ito, A. Govindarajan, H. Ito, and Y. Fong, "Surgical Treatment of Hepatic Colorectal Metastasis Evolving Role in the Setting of Improving Systemic Therapies and Ablative Treatments in the 21st Century," *Cancer Journal,* vol. 16, pp. 103-110, 2010.

[5] E. Norero, N. Jarufe, J. M. Butte, B. Norero, I. Duarte, J. Torres*, et al.*, "Outcome of surgical treatment of liver metastasis from colorectal cancer," *Revista Medica De Chile,* vol. 137, pp. 487-496, 2009.

[6] U. Leung, A. L. Simpson, R. L. C. Araujo, M. Goenen, C. McAuliffe, M. I. Miga*, et al.*, "Remnant Growth Rate after Portal Vein Embolization Is a Good Early Predictor of Post-Hepatectomy Liver Failure," *Journal of the American College of Surgeons,* vol. 219, pp. 620-630, Oct 2014.

[7] M. Nikfarjam, S. Shereef, E. T. Kimchi, N. J. Gusani, Y. X. Jiang, D. M. Avella*, et al.*, "Survival Outcomes of Patients with Colorectal Liver Metastases Following Hepatic Resection or Ablation in the Era of Effective Chemotherapy," *Annals of Surgical Oncology,* vol. 16, pp. 1860-1867, 2009.

[8] L. W. Clements, "Salient Anatomical Features for Robust Surface Registraton and Atlas-Based Model Updating in Image-guided Liver Surgery," Ph.D., Biomedical Engineering, Vanderbilt University, Nashville, 2009.

[9] A. L. Simpson, J. N. Leal, A. Pugalenthi, P. J. Allen, R. P. DeMatteo, Y. Fong*, et al.*, "Chemotherapy-Induced Splenic Volume Increase Is Independently Associated with Major Complications after Hepatic Resection for Metastatic Colorectal Cancer," *Journal of the American College of Surgeons,* vol. 220, pp. 271-280, Mar 2015.

[10] U. Leung, A. L. Simpson, L. B. Adams, W. R. Jarnagin, M. I. Miga, and T. P. Kingham, "Image guidance improves localization of sonographically occult colorectal liver metastases," presented at the SPIE Medical Imaging: Image-Guided Procedures, Robotic Interventions, and Modeling Conference, Orlando, FL, 2015.

[11] L. W. Clements, J. A. Collins, J. A. Weis, A. L. Simpson, W. R. Jarnagin, and M. I. Miga, "Towards validation of model-based deformation correction in image-guided liver surgery via tracked intraoperative ultrasound," *Journal of Medical Imaging,* 2016 2016.

[12] J. A. Collins, J. A. Weis, J. S. Heiselman, L. W. Clements, A. L. Simpson, W. R. Jarnagin*, et al.*, "Improving registration robustness for image-guided liver surgery in a novel human-to-phantom data framework," *IEEE Transactions on Medical Imaging,* p. (in press), 2017.

[13] D. C. Rucker, Y. Wu, L. W. Clements, J. E. Ondrake, T. S. Pheiffer, A. L. Simpson*, et al.*, "A Mechanics-Based Nonrigid Registration Method for Liver Surgery Using Sparse Intraoperative Data," *Ieee Transactions on Medical Imaging,* vol. 33, pp. 147-158, Jan 2014.

[14] A. L. Simpson, P. Dumpuri, J. E. Ondrake, J. A. Weis, W. R. Jarnagin, and M. I. Miga, "Preliminary study of a novel method for conveying corrected image volumes in surgical navigation," *International Journal of Medical Robotics and Computer Assisted Surgery,* vol. 9, pp. 109-118, Mar 2013.