Image Guidance Improves Localization of Sonographically Occult Colorectal Liver Metastases

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ABSTRACT

Assessing the therapeutic benefit of surgical navigation systems is a challenging problem in image-guided surgery. The exact clinical indications for patients that may benefit from these systems is not always clear, particularly for abdominal surgery where image-guidance systems have failed to take hold in the same way as orthopedic and neurosurgical applications. We report interim analysis of a prospective clinical trial for localizing small colorectal liver metastases using the Explorer system (Pathfinder Technologies, Nashville, TN). Colorectal liver metastases are small lesions that can be difficult to identify with conventional intraoperative ultrasound due to echogeneity changes in the liver as a result of chemotherapy and other preoperative treatments. Interim analysis with eighteen patients shows that 9 of 15 (60%) of these occult lesions could be detected with image guidance. Image guidance changed intraoperative management in 3 (17%) cases. These results suggest that image guidance is a promising tool for localization of small occult liver metastases and that the indications for image-guided surgery are expanding.

1. PURPOSE

Colorectal cancer is the third most common cancer diagnosed and the third leading cause of cancer death in the United States with more than 135,000 new cases and 50,000 deaths expected this year.[1] Approximately 50% of patients with colorectal cancer will develop liver metastases.[2] With improvements in surgical technique and use of down-sizing neoadjuvant chemotherapy, up to 20-30% of patients now have resectable disease, with 5-year survival after resection reaching 35-58%.[3,4] Chemotherapy often results in tumor regression, in some cases to the point of "disappearance" on preoperative CT and MRI or at intraoperative exploration with ultrasound (US). However, pathological complete response is uncommon with persistent microscopic disease in 80% of cases.[5] Chemotherapy associated steatosis (fatty changes) is associated with hyperechogenicity of the background liver parenchyma, which further confounds intraoperative US localization of lesions.[6,7] The surgeon is often faced with pre-treatment liver metastases that are difficult to identify in the operating room, with significant clinical implications. Failure to identify and treat these areas of active disease represents a failure of surgical therapy, leading to early disease progression. Our hypothesis is that use of an image guided surgery (IGS) system increases the rate of localizing small colorectal liver metastases over conventional interrogation with intraoperative US.

2. METHODS

Patients are eligible for the study if they have one or more colorectal liver metastases, with at least one of which is $\leq$1.5cm in maximal diameter on preoperative cross sectional imaging, and are undergoing open or laparoscopic liver resection and/or ablation. Final selection of the patient is performed by the attending surgeon based on whether or not the tumor(s) may be difficult to find intraoperatively based on treatment characteristics such as the presence of steatosis and fibrosis (excess connective tissue), chemotherapy regimen (such as hepatic arterial infusion pump), and portal vein embolization.

The FDA approved Explorer system (Pathfinder Technologies Inc., Nashville, TN) was used for all data collection in this study. Aspects of the guidance system are shown in Figure 2: preoperatively, the liver, tumors, and vasculature are segmented from portal-venous phase CT (a) and three dimensional models constructed from the imaging data (b). Intraoperatively, the liver is mobilized and an optically tracked sterile tool (c) is used to digitize the surface of the liver for rigid registration (d). A sterile optically tracked rigid body is attached to the

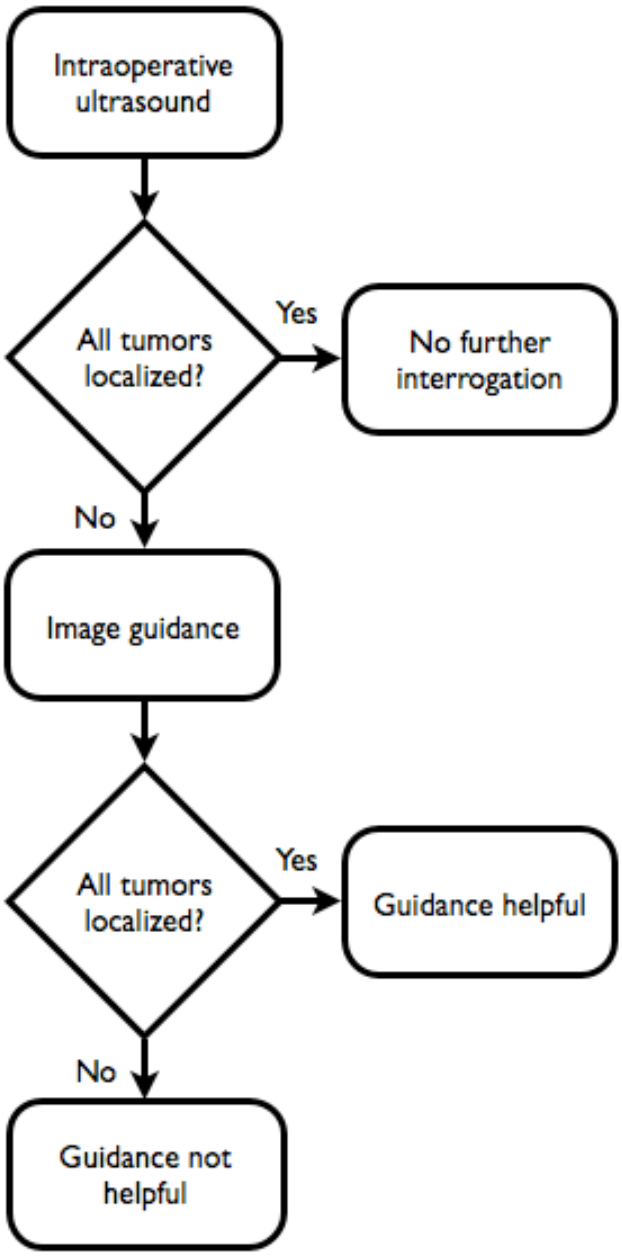

Figure 1. Flowchart depicting intraoperative events in study.

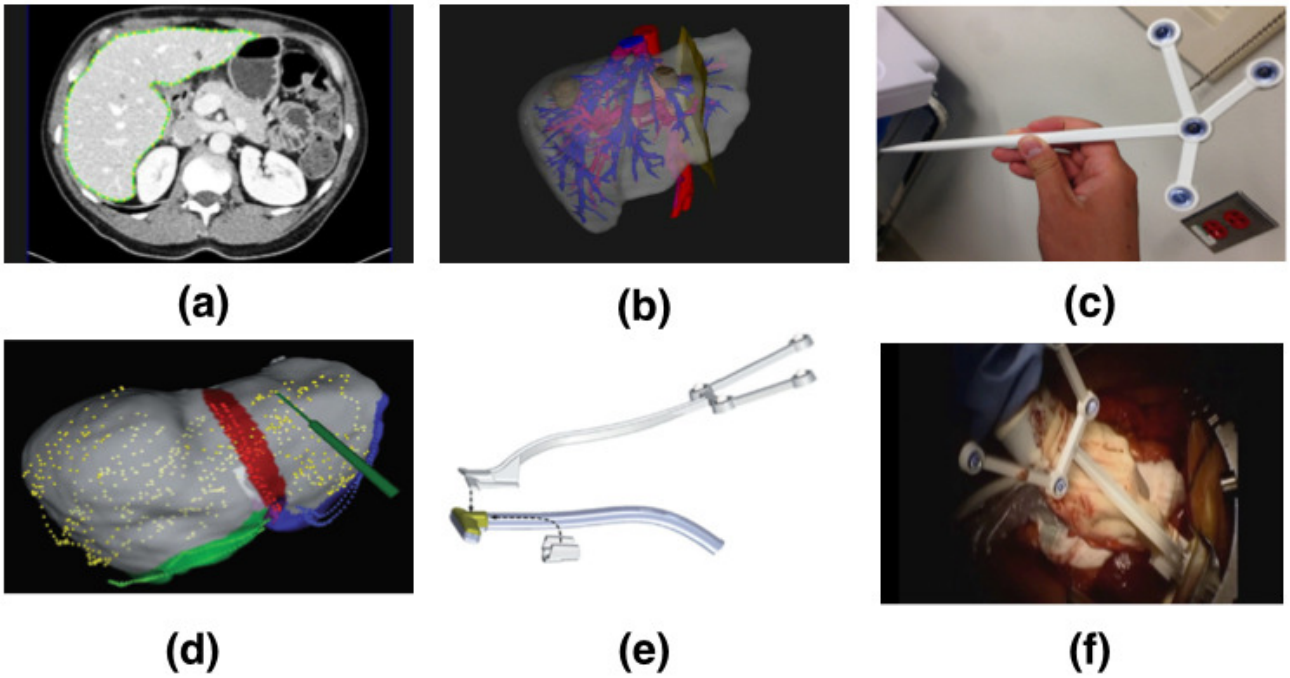

Figure 2. Workflow for Explorer system: (a) image segmentation, (b) preoperative planning and model generation, (c) surgical tool tracking, (d) intraoperative rigid registration, (e) tracking of Ultrasound transducer, and (f) interrogation of liver surface with tracked Ultrasound.

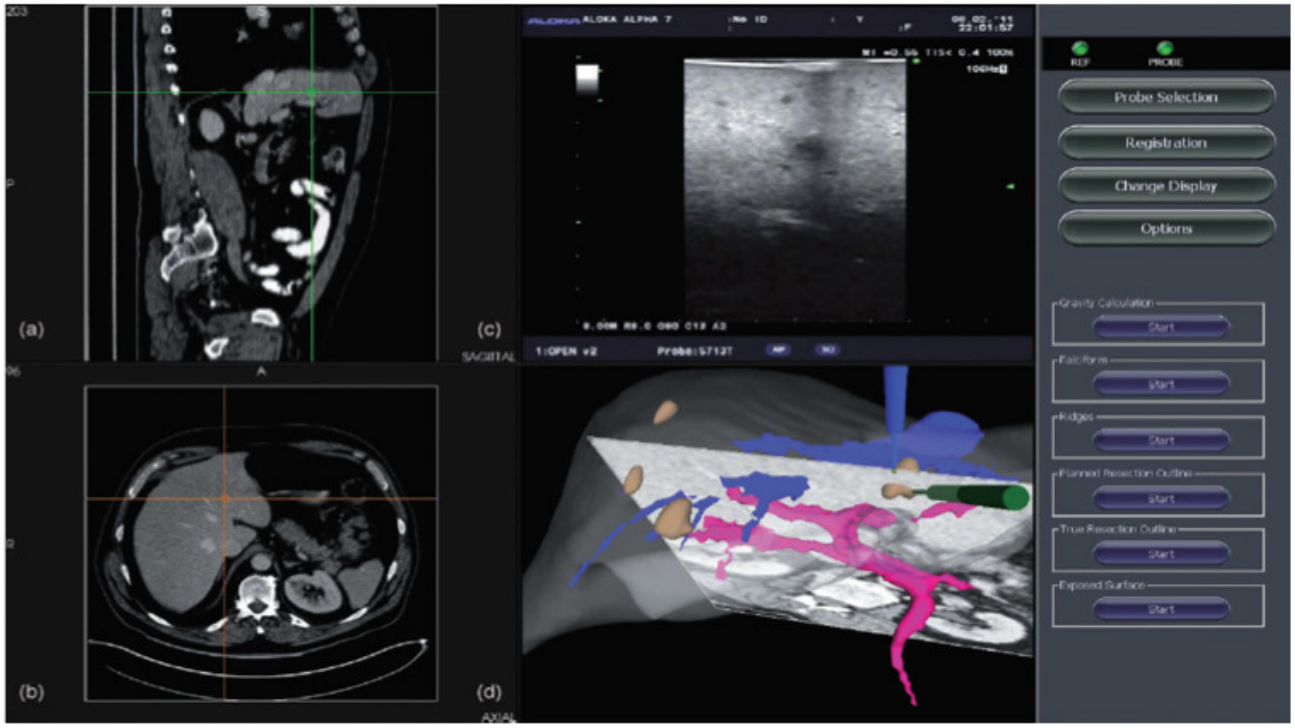

Figure 3. Standard Explorer system display including the cross-sectional views (left), Ultrasound views (top right), and 3D model view (bottom right) during intraoperative use. In this example, the tumor is clearly visible in both the model and Ultrasound views.

Table 1. Summary Statistics

	US[a]	IGS[b]	p-value	Found[c]
Number of tumors	42	9	-	6
Mean tumors size[d], mm	12.8	8.1	0.078	8.5
Proportion perivascular[e]	18/42	3/9	0.720	2/6
Proportion subcapsular[f]	21/42	2/9	0.160	2/6
Duration of pre-op chemo	4.4	7.2	0.051	5.8
Steatosis (clinical/radiological)	4/42	0/6	-	0/6

[a]Tumors interrogated and found with US
[b]Tumors interrogated with US, not found, then identified with IGS
[c]Tumors not found with either US or IGS
[d]Pathological if available, otherwise radiological
[e]Within 10mm of a vessel >5mm in size
[f]Within 10mm of capsule

Ultrasound transducer using a protocol consistent with the manufacturers specifications (e). Intraoperatively, after the liver is exposed and mobilized in preparation for resection, conventional US is used to localized tumors. If tumors are successfully localized, surgery continues. If tumors are not localized, the Explorer image guidance system (Pathfinder Technologies, Nashville, TN) is used to guide the search. Intraoperative workflow for the study is illustrated in Figure 1.

The time spent by the surgeon using the US is recorded. The location, number, size, and sonographic features of any found occult lesions are recorded, as well as the time taken to find each lesion. The primary endpoints of the study are (1) proportion of sonographically occult tumors subsequently found by surgeon using image guidance and (2) proportion of patients where image-guidance was clinically helpful (as determined by surgeon). Fifty patients are targeted for enrollment in the study.

3. RESULTS

Eighteen patients have been enrolled in the study to date. Summary statistics are detailed in Table 1. In total, 57 metastases were interrogated with intraoperative US, with 15 (26%) not localized. Nine metastases were subsequently found with image-guidance. Therefore, image guidance was useful in 9 of 57 (16%) metastases and 9 of 15 (60%) of sonographically occult metastases found by guidance. To date, in 6 of 16 (38%) patients, the image guidance system was required to find a metastasis the surgeon could not otherwise locate. These findings are summarized in Table 2. An example of a tumor successfully localized in the image guidance system, not found initially in US is shown in Figure 4.

Table 2. Summary of study findings

Number of metastases interrogated with intraoperative US, n	57
Time spent on intraoperative US, median (range)	7.0 (2.5-17.5)
Number of occult metastases, n (%)	15 (26)
Number of occult metastases found with IGS, n (5)	9 (60)
IGS changed management, n (%)	3 (17)

4. DISCUSSION

We report interim analysis of a prospective clinical trial assessing whether image guidance can help localize small colorectal liver metastases during resection. We show that for a subset of patients, image-guided surgery is beneficial. As we improve localization accuracy in these systems, by compensating for effects of organ deformation during surgery, we expect to find more indications in support of this technology.

This study is designed to quantify the clinical utility of image guidance in liver surgery. Assessing the direct benefit of image-guided surgery to clinical care is a fundamental challenge in surgical navigation, one largely

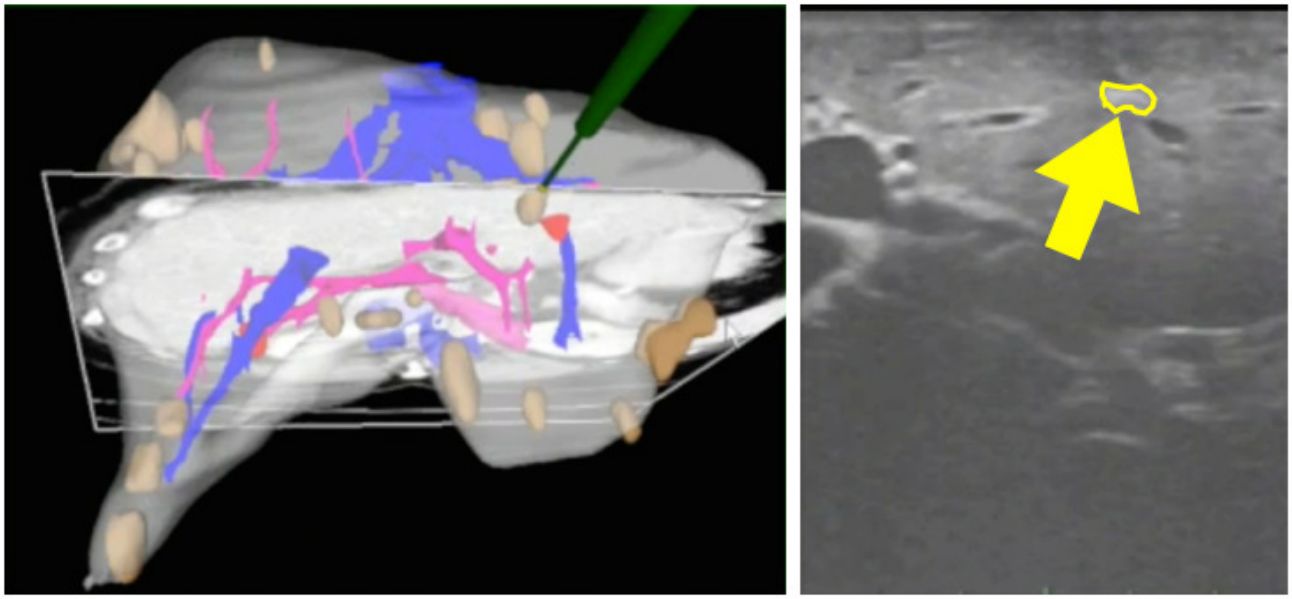

Figure 4. Tumor successfully located with guided ultrasound: (left) green probe indicates tumor in CT on the image-guidance display and (right) yellow arrow indicates tumor.

unaddressed in the literature. This is likely because of the difficulty in choosing an appropriate control group and primary endpoints for randomized clinical trials. We describe a prospective trial wherein clinically relevant endpoints are assessed. Our preliminary analysis suggests that image guidance is useful for localizing small, sonographically occult colorectal liver metastases.

5. CONCLUSIONS

Image-guidance is a promising tool for localizing small colorectal liver metastases.

6. ACKNOWLEDGEMENTS

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