Liver Planning Software Accurately Predicts Postoperative Liver Volume and Measures Early Regeneration

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BACKGROUND: Postoperative or remnant liver volume (RLV) after hepatic resection is a critical predictor of perioperative outcomes. This study investigates whether the accuracy of liver surgical planning software for predicting postoperative RLV and assessing early regeneration.

STUDY DESIGN: Patients eligible for hepatic resection were approached for participation in the study from June 2008 to 2010. All patients underwent cross-sectional imaging (CT or MRI) before and early after resection. Planned remnant liver volume (pRLV) (based on the planned resection on the preoperative scan) and postoperative actual remnant liver volume (aRLV) (determined from early postoperative scan) were measured using Scout Liver software (Pathfinder Therapeutics Inc.). Differences between pRLV and aRLV were analyzed, controlling for timing of postoperative imaging. Measured total liver volume (TLV) was compared with standard equations for calculating volume.

RESULTS: Sixty-six patients were enrolled in the study from June 2008 to June 2010 at 3 treatment centers. Correlation was found between pRLV and aRLV ($r = 0.941$; $p < 0.001$), which improved when timing of postoperative imaging was considered ($r = 0.953$; $p < 0.001$). Relative volume deviation from pRLV to aRLV stratified cases according to timing of postoperative imaging showed evidence of measurable regeneration beginning 5 days after surgery, with stabilization at 8 days ($p < 0.01$). For patients at the upper and lower extremes of liver volumes, TLV was poorly estimated using standard equations (up to 50% in some cases).

CONCLUSIONS: Preoperative virtual planning of future liver remnant accurately predicts postoperative volume after hepatic resection. Early postoperative liver regeneration is measureable on imaging beginning at 5 days after surgery. Measuring TLV directly from CT scans rather than calculating based on equations accounts for extremes in TLV. (J Am Coll Surg 2014;219: 199–207. © 2014 by the American College of Surgeons)

During the past several years, partial hepatectomy has emerged as the most effective and the only potentially curative therapy for many primary and secondary hepatic tumors.[1,2] The therapeutic advantage of resection over other treatments is now clear, but has only manifested as the marked improvements in safety have been realized.

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Abbreviations and Acronyms

aRLV = actual remnant liver volume
BSA = body surface area
CI = confidence interval
IQR = interquartile range
MSKCC = Memorial Sloan-Kettering Cancer Center
pRLV = planned remnant liver volume
TFLV = total functional liver volume
TLV = total liver volume
UPMC = University of Pittsburgh Medical Center

Full recovery from major hepatic resection requires a healthy, well-perfused liver remnant that is capable of regenerating to its preresection volume. A better appreciation of the adequacy of the future liver remnant size and quality has represented an important safety advance in hepatic resectional surgery. Several studies have shown that the percentage of functional liver parenchyma remaining after major hepatic resection is an important predictor of postoperative hepatic dysfunction and morbidity.[3-6]

In the past, liver volumetry was calculated either by using equations involving height and weight[7,8] that fail to account for individual variability, or by manually designating liver parenchyma and tumor boundaries from cross-sectional imaging studies,[3,9] which is time consuming. In the last decade, automated and semi-automated methods of demarcating the liver from neighboring structures have been the subject of intense investigation,[10] with some clinical adoption.[3,11,12] Software tools now exist for computing hepatic volumetry and defining surgical resection margins on virtual anatomy[13,14]; however, whether these utilities accurately predict postoperative volume is an unresolved question. Studies that correlate virtual resection volume with the volume of the resected mass do so by weighing the mass after resection and applying a conversion factor from weight to volume (1 g = 1 mL)[15] or by acquiring postoperative scans more than a week after surgery,[11] after volume changes might have occurred.

This multicenter study evaluates the accuracy of surgical planning software for defining virtual cutting planes for hepatic resection. The primary aim was to correlate the volume of the virtual remnant and the volume of the actual remnant, where the postoperative volume is computed directly from postoperative imaging scans as a true measure of accuracy; the secondary aim was to assess early liver regeneration patterns in the early postoperative period.

METHODS

The data reported in this study were collected during a prospective clinical trial (ClinicalTrials.gov ID: NCT00782886) sponsored by Pathfinder Therapeutics Inc., supported by a grant from the Small Business Innovative Research fund provided by NIH/National Cancer Institute, titled "Evaluation of Image-Guided Liver Surgical System for Resection of Liver Cancer," and conducted at 3 treatment centers: University of Florida, Gainesville, Memorial Sloan-Kettering Cancer Center (MSKCC), and University of Pittsburgh Medical Center (UPMC) from June 2008 through June 2010. This was a clinical trial aimed at assessing the utility and safety (phase II equivalent) of the Pathfinder intraoperative image guidance system. Institutional Review Board authorization was obtained from the participating institutions before the study. Demographic, laboratory, histopathologic, operative, perioperative, and survival data were collected prospectively and analyzed retrospectively. Patients received standard contrast-enhanced preoperative MRI or CT scans, as is standard practice at the participating institutions. As part of the IRB protocol, patients received a postoperative CT scan in the immediate days after surgery. Complications were graded according to the Common Toxicity Criteria from the National Cancer Institute.

Patient selection

Candidates for resection of malignant or benign tumors with measurable disease on preoperative imaging and surgical treatment requiring removal of at least 1 anatomical segment were selected for the study. Patients with cirrhosis of the liver classified as Child-Pugh score B or C, thrombocytopenia, or renal insufficiency (defined as creatinine >2.5 mg/dL), were excluded from consideration. The preoperative evaluation, intraoperative management, and conduct of the operation at the 3 centers have been described previously.[16-18]

Preoperative planning software

Scout Liver (Pathfinder Therapeutics) is commercially available preoperative planning software that provides 3-dimensional visualization and measurement of structures of interest in the liver using CT and MRI imaging studies. The software allows the user to manually or semi-automatically segment the liver, intrahepatic vessels, and tumors. A sample Scout Liver after segmentation is depicted in Figure 1. Specific surgical strategies can be virtually defined by delineating resection lines and ablation paths. The software provides volumetric measurements of functional liver volume, remnant liver volume, and lesions as well as measurements of the planned resection. The software allows the user to query, choose, and pull scans directly from the patient records and communication system, requires 5 to 15 minutes to run and then

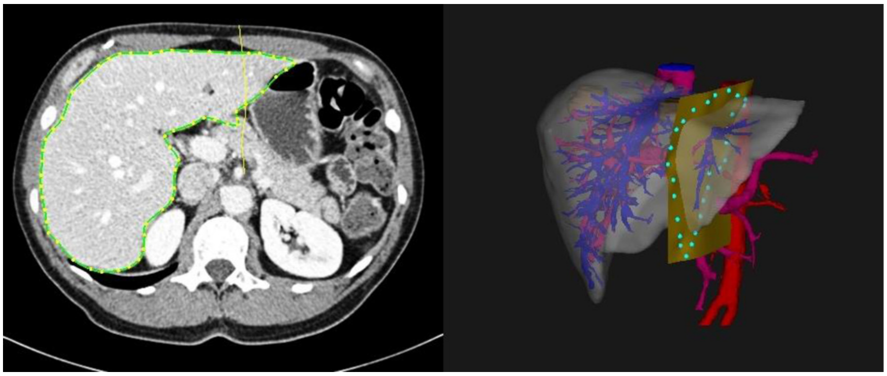

Figure 1. Sample data from Scout Liver planning software: (left) CT image with boundaries of organ indicated by green contour and (right) 3-dimensional model of organ with hepatic (red) and portal (blue) venous systems, tumor (brown), and resection plane.

up to 15 minutes of user interaction without the need for a radiologist.

The accuracy and repeatability of the segmentation results were independently evaluated at the Catholic University of Louvain in Belgium and were found to be more consistent but as accurate as radiologists manually designating contours.[19] The algorithm for semi-automatically designating the liver contours was compared with state-of-the-art techniques from several academic institutions and scored highest overall with respect to accuracy when compared with manual techniques.[10] The underlying algorithm used by the software for determining the volume of a 3-dimensional object generated from contours in CT is based on a well-established technique[20] used in most modern software packages and radiologic workstations, so one would not expect software to compute more or less accurate volumes than manual techniques but rather similar volumes.

Pre- and postoperative liver volumetry measurements

The Scout Liver software calculated the patient's total liver volume (TLV) and tumor volume. The total functional liver volume (TFLV) was calculated by subtracting the tumor volume from the TLV. Using the planning software, a virtual resection was performed according to the surgical strategy for each patient and the planned remnant liver volume (pRLV) was calculated using the software, based on the virtual resection. The relative remnant liver volume was expressed as: %RLV = pRLV/TFLV $\times$ 100. Immediately after surgery, the virtual plan was modified to reflect the true resection in the event that the surgeon changed the operative plan. The actual remnant liver volume (aRLV) was calculated from postoperative CT acquired within 5 days of surgery (if clinically warranted, this scan could be deferred for up to 2 weeks after surgery) and measured using the surgical planning software. The relative change from the planned to the actual remnant liver volume was calculated as (aRLV $-$ pRLV)/aRLV $\times$ 100.

The patient's body surface area (BSA) was calculated using a formula by Dubois and Dubois[21]: BSA (m^2) = weight (kg)$^{0.425}$ $\times$ height (cm)$^{0.725}$. For comparison with the Scout Liver software, the patient's TLV was calculated using 3 formulas: Vauthey and colleagues[7] (based on BSA): TLV (cm^3) = $-794.41 + 1{,}267.28 \times$ BSA (m^2), Vauthey and colleagues (based on weight): TLV (cm^3) = $191.80 + 18.51 \times$ weight (kg), and Urata and colleagues[22] (based on BSA): TLV (cm^3) = $706.2 \times$ BSA (m^2) $+ 2.4$.

Statistical analysis

Correlation and multiple linear regression analyses were conducted to examine the relationship between the postoperative volume and the timing of the postoperative scan, treatment center, resection extent, and type of preoperative imaging (CT or MRI) as potential predictors. A regression line with aRLV as the dependent variable (y-axis) and pRLV (as predictor) was derived, and the correlation coefficient (Pearson's) was calculated. A multiple linear regression modeled the relationship between the aRLV and the pRLV and the timing of the postoperative scan. Segmented regression can help identify change points (also called breakpoint, threshold, or transition point) in the relationship between the response and some explanatory variables in a regression model.[23] The change point is introduced as a parameter to the regression model along with intercepts and slopes for the subsets before and after the change point. All the coefficients are simultaneously estimated using least squares subject to the constraint that the 2 lines so estimated connect at the change point. After all of the coefficients are estimated, the difference between the 2 slopes (before and after the change point) is compared using a maximally selected test statistic.[24] The technique was used here to assess a possible threshold value in the relative difference between pRLV and aRLV (response), based on the timing of the postoperative scan and extent of resection (explanatory variables), to suggest an influence of hepatic regeneration. A mixed-effects model was used to analyze differences due to treatment center and type of preoperative imaging (CT or MRI). The 95% confidence intervals (CIs) for the predicted values were calculated for each regression. An analysis of variance was used to compare TLV computed using the 4 methods described here with respect to treatment center. A p value <0.05 was considered to indicate significant differences. All statistical analyses were performed with a software package (SPSS, IBM Corporation).

RESULTS

Treatment centers, demographics, operative procedures, and complications

During the 2-year study period, 86 patients were approached for participation and enrolled in the study. Of the original cohort, 20 patients did not have pre- and postoperative scans: 5 patients withdrew consent before surgery, 3 patients were deemed unresectable due to extrahepatic disease, 1 patient was admitted to ICU before surgery, 4 patients refused the postoperative scan, 2 patients did not receive the postoperative scan due to clinical reasons, and 5 patients had logistic/equipment issues at the time of surgery, as detailed in Figure 2. Sixty-six patients had pre- and postoperative scans and were therefore included in our analysis: 20 (30%) patients from UPMC, 34 (52%) from MSKCC, and 12 (18%) from University of Florida. Patient characteristics are summarized in Table 1. Thirty-three (50%) patients were men and the median age was 54.0 years (interquartile range [IQR] 44 to 66 years). Median BMI was 26.9 (IQR 23.1 to 32.0).

Of the 66 enrolled patients, the majority underwent right hepatectomy (29 patients [44%]), followed by left hepatectomy (9 patients [14%]), left lateral sectionectomy (8 patients [12%]), atypical resections (7 patients [11%]), extended right hepatectomy (6 patients [9%]), right posterior sectionectomy (3 patients [5%]), segmentectomy (3 patients [5%]), and multiple wedge resections (1 patient [2%]). The extent of resection by mean relative remnant liver volume is summarized in Table 2.

All patients underwent resection with no noteworthy intraoperative events. Of the 66 patients, 23 had a total

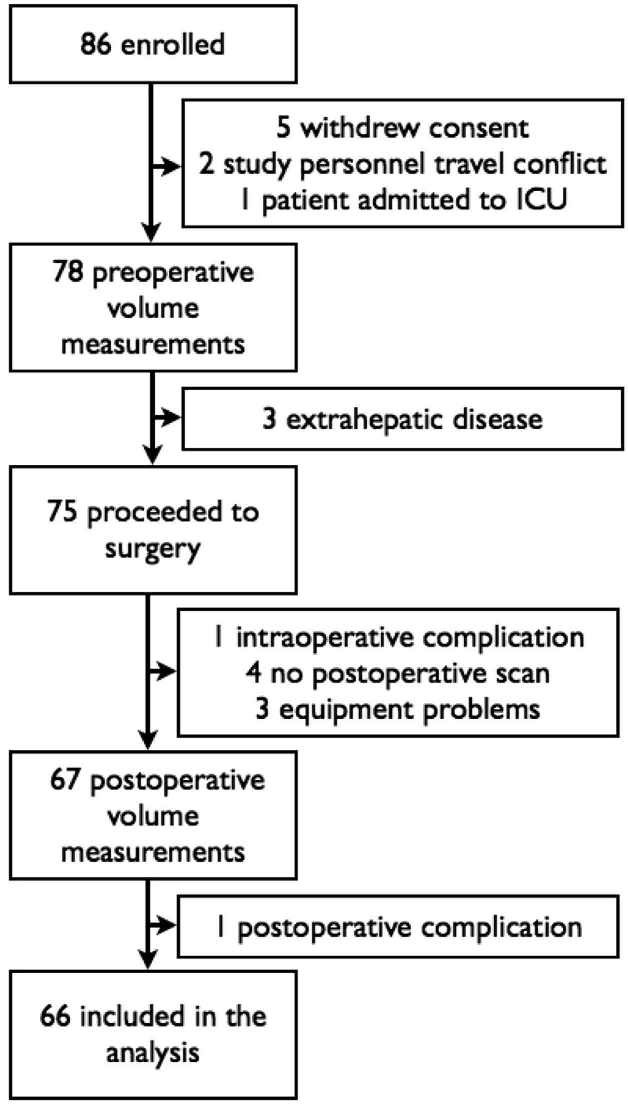

Figure 2. Trial profile.

of 29 complications, for a complication rate of 35%. Nineteen major complications (Common Toxicity Criteria grade $\geq$3) were observed in 16 patients, for a major complication rate of 24%. Major complications included perihepatic seroma, pleural effusion, deep-vein thrombosis (3 patients), respiratory distress, acute respiratory failure, infection (2 patients), hemoglobin, would infection, abdominal hemorrhage, renal failure, and fascial wound dehiscence, and sepsis with multi-organ failure. One patient died on postoperative day 22 due to heart failure.

Mean TLV calculated by the Scout software was 1,816 $\pm$ 596 cm^3; mean pRLV was 1,055 $\pm$ 508 cm^3, and mean aRLV was 1,144 $\pm$ 506 cm^3. Mean tumor volume measured with the Scout software was 89 $\pm$ 200 cm^3. By comparison,

Table 1. Clinicopathologic Factors of Patients Who Underwent Resection after Preoperative Planning (n = 66)

Clinicopathologic factor	All patients
Treatment center, n (%)	
UPMC	20 (30)
MSKCC	34 (52)
UF	12 (18)
Age, y, median (IQR)	54 (44–66)
Sex, n (%)	
Male	33 (50)
Female	33 (50)
Weight, kg, median (IQR)	77 (61–92)
Height, cm, median (IQR)	169 (160–176)
BMI, median (IQR)	26.9 (23.1–32.0)
Body surface area, m^2, median (IQR)	1.9 (1.7–2.1)
Scout TLV, cm^3 (mean ± SD)	1,816 ± 596
Planned RLV, cm^3 (mean ± SD)	1,055 ± 508
Actual RLV, cm^3 (mean ± SD)	1,144 ± 506
%RLV* (mean ± SD)	61.1 ± 21.5
Tumor volume, cm^3 (mean ± SD)	89 ± 200
Tumor(s), n, median (IQR)	1 (1–3)
Postoperative CT timing, d, median (IQR)	5 (3–6)
Mortality, n (%)	1 (2)
Complications, n (%)	23 (35)
Margin status, n (%)	
Negative	59 (89)
Positive	7 (11)
Diagnosis, n (%)	
Metastatic CRC	36 (55)
Hepatocellular cancer	8 (12)
Cholangiocarcinoma	8 (12)
Benign	7 (11)
Other†	7 (11)

*%RLV= pRLV/total functional liver volume × 100.
†Gastrointestinal stromal tumor, anal cancer, liver angiosarcoma, breast cancer, hemangiopericytoma, gallbladder cancer, and germ cell carcinoma.
CRC, colorectal cancer; IQR, interquartile range; MSKCC, Memorial Sloan Kettering Cancer Center; pRLV, predicted remnant liver volume; RLV, remnant liver volume; TLV, total liver volume; UF, University of Florida; UPMC, University of Pittsburgh Medical Center.

mean TLV calculated using the Vauthey formula based on weight[7] and based on BSA,[8] and the Urata formula[22] were 1,669 ± 451 cm^3, 1,629 ± 419 cm^3, and 1,331 ± 214 cm^3, respectively. No significant differences were found between the liver volume as determined by the Scout software and these calculation methods; however, the formulas do not adequately capture the extremes of the study group. For example, the largest TLV measured by the software was 3,526 cm^3; by contrast, for the same patient, the formulas predicted TLV values of 1,562 cm^3 (Vauthey weight), 1,589 cm^3 (Vauthey BSA), and 1,322 cm^3 (Urata), severely underestimating the volume. Similarly, the smallest TLV measured by the software was 788 cm^3; the formula-predicted TLVs were 923 cm^3 (Vauthey weight), 831 cm^3 (Vauthey BSA), and 918 cm^3 (Urata).

Table 2. Extent of Resection Therapy by Mean Relative Remnant Liver Volume for 66 Patients

Type of resection	n	%RLV,* mean ± SD
Extended right hepatectomy	6	39.7 ± 3.5
Right hepatectomy	29	43.2 ± 7.2
Right posterior sectorectomy	3	73.9 ± 2.4
Left hepatectomy	9	75.2 ± 8.4
Left lateral segmentectomy	8	81.8 ± 9.9
Segmentectomy	3	87.8 ± 15.0
Atypical resections†	7	89.7 ± 3.8
Multiple wedge resections‡	1	95.2 ± 0.0

*% RLV = predicted remnant liver volume/total functional liver volume × 100.
†One segment resected.
‡Two segments resected.
RLV, remnant liver volume.

The timing of the postoperative scans varied based on the clinical condition of the patients in some cases and regulatory issues at one study site mandated outpatient postoperative scans. The postoperative scans were acquired at a median of 5 days after resection (IQR 3 to 6 days). With respect to timing of the postoperative scan, 52 (79%) scans were acquired within 7 days of surgery: 15 of 20 scans at UPMC (75%), 25 of 34 scans at MSKCC (74%), and 12 of 12 scans at University of Florida (100%). Nine scans (14%) were acquired 7 to 14 days after surgery: 3 of 20 at UPMC (15%) and 6 of 34 at MSKCC (18%). The remaining scans were acquired more than 14 days after surgery: 2 of 20 at UPMC (10%) and 3 of 34 at MSKCC (9%).

Planned vs actual resection

There was a strong positive correlation between the aRLV and the pRLV (aRLV = 0.939 × pRLV + 157.2; r = 0.941; $p < 0.001$) (Fig. 3A). The model accounted for approximately 89% of the variation in aRLV. A multiple linear regression modeled the relationship between the aRLV and the pRLV and the timing of the postoperative scan. Planned RLV and the timing of the scan were positively correlated with aRLV ($r = 0.953$; $p < 0.01$) (Fig. 3B). This model accounted for approximately 91% of the variation in the postoperative volume. Points above the regression line in Figure 3B indicate positive volume change; black points (patients with scans acquired more than 7 days after surgery) appear above and yellow points (patients with scans acquired within 1 day of surgery) lie below the line.

A mixed-effects model was constructed with treatment center as a random effect and complications with

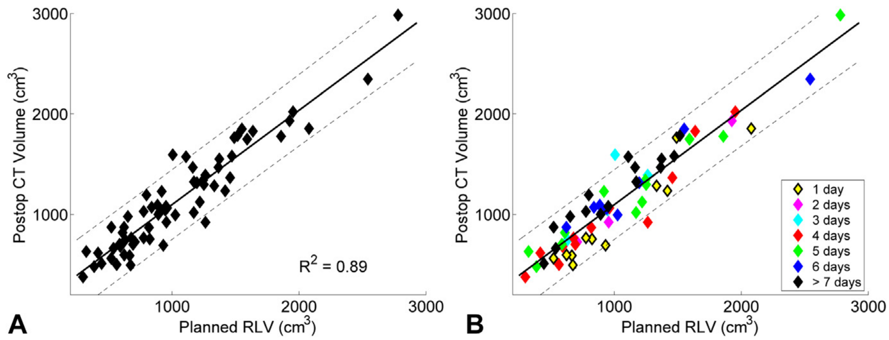

Figure 3. (A) Scatterplot of the regression analysis with the planned remnant liver volume (RLV) (virtual resection) and the actual RLV (postoperative CT volume) with the 95% confidence interval. There is good correlation between the planned RLV (pRLV) and actual postoperative volume (aRLV) (aRLV = 0.939 × pRLV + 157.2; $p < 0.001$). The p value is testing whether the slope of the line is zero. (B) Scatterplot colored by the timing of the postoperative CT. Note that the data points of earlier scans fall below the line and later scans above the line.

Common Toxicity Criteria grade >3, the type of preoperative imaging (CT or MRI), RLV, and number of days after surgery for the postoperative scan treated as fixed effects. Treatment center, complications, and the type of preoperative imaging did not contribute to the multiple linear regression model.

Assessment of postoperative regeneration

The timing of the postoperative scan was assessed in an attempt to identify a pattern for early postoperative liver regeneration and potentially inform early prediction of hepatic dysfunction. Computing the relative change in liver volume from planned to actual (postoperative) and then ordering this value by timing of the scan is illustrated in Figure 4. Segmented regression[23] partitioned the relative liver volume change by the timing of the postoperative scan, with a threshold of 8 days (95% CI, 5−11 days), so that the liver growth rates before and after 8 days were significantly different ($p < 0.01$). The 95% CI indicates measurable regeneration at as early as 5 days. This suggests that liver regeneration begins immediately after resection and stabilizes after 8 days (Fig. 5A). When the extent of resection is factored into the segmented regression, the liver growth stabilizes at 6 days (95% CI, 4−9 days; $p < 0.01$ for comparing growth rates before and after 6 days) for major resections (4 or more segments resected) (Fig. 5B). The relative liver volume change in the first 6 days is significantly higher for major resections as compared with minor ones ($p < 0.01$). No significant differences were found with respect to complications, so hepatic dysfunction could not be assessed.

DISCUSSION

Accurate preoperative assessment and planning are critically important for hepatic resection surgery, not only to ensure appropriate management of the neoplastic disease but, as important, to ensure the presence of an adequate liver remnant. The importance of the latter for major hepatic resections is clear, with several reports showing the close association between future liver remnant volume and perioperative outcomes. Cross-sectional imaging studies remain the predominant modality used in this process, although 3-dimensional planning software is being used with greater frequency.

The principal finding of this study is that postoperative liver volume can be accurately predicted using preoperative planning software; there was a very strong positive correlation between the pRLV and the aRLV measured from postoperative scans ($r = 0.941$; $p < 0.001$). Other

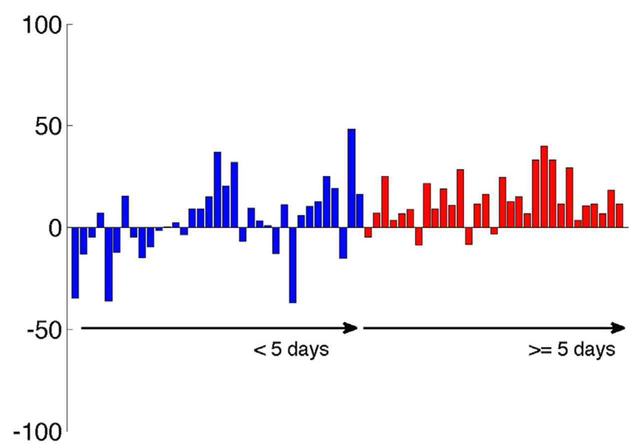

Figure 4. Plot showing the relative percent change from the planned to the actual remnant liver volume, in increasing order by number of days after surgery in which postoperative CT was acquired beginning with 1 day (far left) to more than 5 days (far right, in red). It appears that as soon as 5 days after surgery, the liver shows some measurable volume increases.

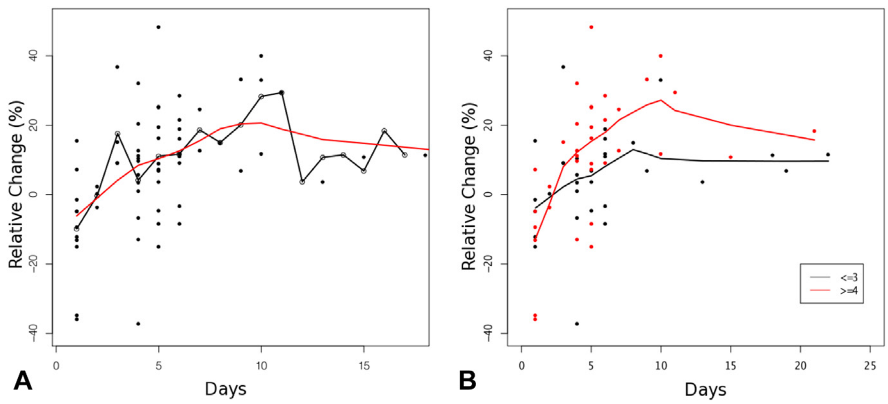

Figure 5. Relative change from the planned to the actual resection plotted against the timing for the postoperative scan. (A) The black dots represent the data, the black line is the mean relative change for each day, and the red line represents the smoothed mean.[25] (B) The red dots represent major resections (>4 segments resected) and the black dots the minor resections (<3 segments resected). The lines represent the smoothed means for each group. Relative change = (actual remnant liver volume − planned remnant liver volume)/actual remnant liver volume × 100.

studies that assess the accuracy of virtual planning tools do so by comparing the volumes measured by the software with manual measurements,[19,26] weighing the resected mass and applying a conversion factor from weight to volume,[15,27] or comparison with postoperative images acquired more than a week after surgery.[11,28] The unique aspect of this work is the very early time after surgery when the postoperative scans were acquired (median 5 days; IQR 3 to 6 days). Accuracy was assessed by directly comparing the planned and true volumes segmented using the same software with images from the same imaging protocol to avoid potential errors in RLV comparisons between 2 different modalities. One limitation of the study is that the planned future liver remnant can vary from the exact transection plane carried out in surgery. The planned resection plane was revisited after the procedure in this study to account for changes in resection strategy, but given that the liver volume in the postoperative scans was highly correlated with the planned volume, this effect was likely minimized.

Results also underscore potential inaccuracies in the determination of liver volumes using calculation-based methods, which were inaccurate at the extremes of the size range. These calculations are based on studies of the correlation between TLV measured from CT scans related to BSA and weight.[7,22,29] The formulae were derived from regression lines fit to these data. Inaccuracies are due to the fact that not all individuals fall on this line; some have higher or lower than average liver volumes. This is evidenced in the original studies, where outliers are visible on the regression plots. The calculation-based approaches represent an easy method to predict standardized liver volumes but do not necessarily capture volumes at the extremes of the size range.

Using the planning software for resection planning and future liver remnant volume calculation has several advantages over the conventional technique. The software derives measurements from cross-sectional 3-dimensional imaging from CT or MRI rather than from 2-dimensional images, which are less accurate due to missing information in 1 dimension for volumetric evaluation. For example, Pomfret and colleagues showed that CT angiography overestimated liver graft weight by nearly 10%.[30] Modern radiologic workstations also derive measurements from 3-dimensional images; the accuracy of the Scout software is in line with such systems.[19] The primary advantages of the software are with respect to the automation and ease of use. In our experience, complete processing from pulling the images from institutional storage to generating 3-dimensional models of the liver, tumors, venous structures, and resection boundaries requires 30 minutes (with some inactive time), which is an improvement over other software, which can take up to 2 hours.[13] The Scout software requires limited technical and medical knowledge (basic medical knowledge is required for designating structures for initialization of segmentation algorithms and determination of tumors); it is useful to have a clinician (radiologist or surgeon) verify virtual planning performed by an operator. Although not a replacement for radiologic expertise, the software represents a mechanism by which image volumes can be pulled from patient records and communication system and assessed on any institutional workstation without a radiologist. One of the benefits of planning software in general (be it Scout or another software package) is the ability to visualize in 3 dimensions the precise structure of the tumor location relative to the surrounding major vascular and biliary structures and to determine whether complete extirpation of the disease is possible and maintain an adequate liver remnant volume with intact vascular inflow and outflow and biliary drainage.[13] Without planning software, however, it can be difficult to obtain this information in a manner that optimally facilitates the resection because the surgeon must undertake the complex mental task of reconstructing 3-dimensional image volumes from 2-dimensional slices. Planning software is an effective way to measure hepatic volumetry and can be helpful in assessing pre and post-embolization changes and long-term postoperative liver generation: potential topics for additional research.

Hepatic regeneration is a critical process after resection, but remains incompletely defined. For nearly 30 years, CT volumetry has been used to study liver regeneration after major hepatic resection for liver donation and resection of malignant tumors.[31-33] The rate of hepatic regeneration in normal livers is thought to start with a rapid increase in the first 2 weeks after surgery, followed by a decrease (possibly due to reduction in edema), and a slow and steady increase,[33,34] and is influenced by liver function[31,34,35] and obesity.[36] Whether the extent of resection correlates with the regeneration rate is debatable.[28,34] Studies of early liver regeneration (1 week after surgery), and particularly analyses of regeneration immediately after surgery, are rare.[30,33,35] In this study, the mean remnant was 58% of the original volume at the time of surgery and 64% of the original volume by the first postoperative scan, which indicates earlier regeneration than the 28% to 64% volume regeneration within 2 weeks of surgery reported in other studies.

Although earlier studies have demonstrated liver regeneration in the week after resection, the current study quantifies this by providing convincing evidence that measurable changes in remnant liver volume, using contemporary imaging techniques, begin approximately 5 days after surgery ($p < 0.01$) and begin at 6 days in major resections ($p < 0.01$). The timing of the postoperative scan in the study cohort can influence this cutoff value (median 5 days, IQR 3 to 6 days). However, because early postoperative scans are not the standard of care, scans from a more appropriate time frame are unavailable for study. This early phase of liver regeneration accounts for the large majority of the size increase and would therefore appear to be the most critical. Whether assessment of the early regenerative process can predict perioperative outcomes is unknown. In the current study, there was no clear demonstration that perioperative morbidity adversely impacted regeneration in the early stages; there were no cases of liver failure in this patient cohort and a relatively low complication rate. This might be due to patient selection in the context of the clinical trial; patients were generally healthy with lower-risk resections but a definitive conclusion in this regard will require a larger, more comprehensive analysis.

CONCLUSIONS

This study demonstrates that preoperative virtual planning of the future liver remnant accurately predicts postoperative volume after hepatic resection. Liver volume calculations using the Scout liver software represent direct volume measures and therefore account more fully for patients at the extremes of liver size ranges. Early postoperative liver regeneration is observable and measureable on imaging beginning 5 days after surgery.

Author Contributions

Study conception and design: Miga, Stefansic

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Analysis and interpretation of data: Simpson, Jarnagin, Gönen

Drafting of manuscript: Simpson, Jarnagin

Critical revision: Geller, Hemming, Clements, D'Angelica, Gönen, Zendejas, Miga, Stefansic

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