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Liver Surface Nodularity for Staging Hepatic Fibrosis on CT: A Comparative Study of Liver Segmenters

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Introduction/Background

Cirrhosis is the 12th leading cause of death in the US, and liver fibrosis can be caused by metabolic disorders, alcoholism, and Hepatitis B/C virus. Earlier stages (METAVIR F0 – F2) are reversible with therapy, but later stages (F3 - advanced fibrosis and F4 - cirrhosis) are irreversible. Liver Surface Nodularity (LSN) score, a non-invasive CT-based biomarker that measures the left hepatic lobe surface smoothness, can distinguish later fibrosis stages. However, it depends on a precise liver segmentation.

Methods/Intervention

480 patients underwent CT imaging at Institution-A with fibrosis (METAVIR) staged using biopsy. An internal deep learning tool (INT) segmented the full liver and 8 Couinaud segments. The public TotalSegmentator (TS) tool also segmented the liver. The extents of Couinaud segments 2 and 3 were found. A fully automated image analysis technique detected the liver surface in each 2D slice, and a smooth spline (4th order) was fit to it. The LSN score was the mean distance between the detected surface and fit spline, and higher scores indicated worsening fibrosis. Youden indices were used to find the optimal LSN cutoffs for each fibrosis stage. ROC curves by INT for advanced fibrosis (F3-4 vs. F0-F2) and cirrhosis (F4 vs. F0-3) were compared against TS. An AUC below 0.6 was considered clinically ineffective.
Results/Outcome
AUCs were similar between INT and TS for prediction of cirrhosis (F4, 87.8% vs. 88.7%, p = .143) and advanced fibrosis (≥ F3, 82.5% vs. 83.9%, p = .381). A statistical bootstrap test revealed no differences between the two tools for all three clinically important stages. But the specificity was higher with INT for advanced fibrosis (79.5% vs. 65.1%) and significant fibrosis (73.3% vs. 49.5%), while being comparable for cirrhosis (79.5% vs. 78.4%). Both INT and TS had good agreement (R^2 of 0.8) of computed LSN scores.

Conclusion

Both the internal tool and TotalSegmentator attained comparable performance for fibrosis staging. However, TotalSegmentator did not achieve high specificity.

Statement of Impact

Both INT and TS tools can predict the fibrosis stage in ~45 seconds compared to the ~2 minutes needed to manually measure the LSN in a CT volume. They show promise for population-based studies.

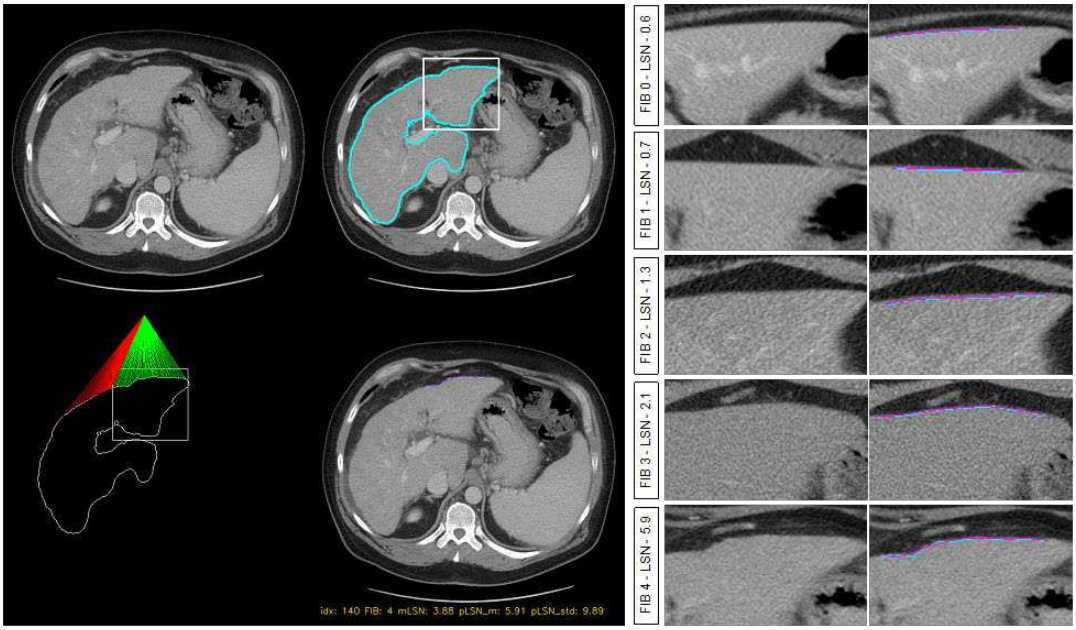

Fig. 1 A fully automated pipeline for measuring the liver surface nodularity (LSN) is described. The liver (cyan, left panel, top right) was segmented by either the internal tool or TotalSegmentator. The extents of the Couinaud segments 2 and 3 were determined (white box), its centroid was found, and projected to the first row of each slice that contained that liver segment. Stemming from this point, radial lines of a length of 512 pixels were cast in the angular range [0, 180] degrees to intersect with the full binary liver segmentation and find the liver surface (green lines). Any points detected along the liver surface that fell outside the extent of the Couinaud segments were discarded (red lines). The remaining points were stitched together to form a curve that ran along the liver edge. The curve was also trimmed by 2 mm to account for any liver fissures (Falciform ligament). Figures on the right show the original CT slice cropped to the left hepatic lobe, and the overlay of the detected liver surface (cyan) and the spline (magenta) that was fit to this surface. The LSN score is the mean distance between the detected and fit surfaces. Note that as the fibrosis stage increases, there is a corresponding increase in the liver surface nodularity

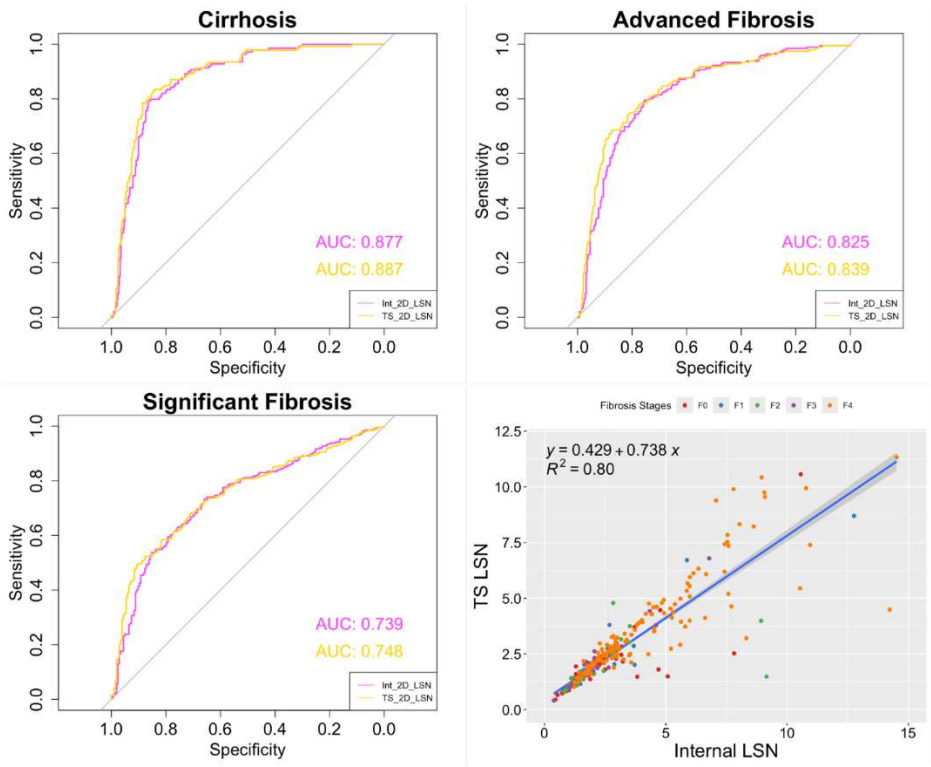

Fig. 2 Comparison of the ROC curves computed by TotalSegmentator (TS) and the internal (INT) tools for Cirrhosis (p = 0.143), Advanced Fibrosis (p = 0.381), and Significant Fibrosis (p = 0.221). There were no significant differences between the two tools for the different liver fibrosis stages. The linear regression plot is also shown in the bottom right corner. An R^2 of 0.8 indicated good agreement between the LSN scores computed by TS and the internal tool

Fibrosis Stage	AUC		Sensitivity		Specificity		LSN Cutoff		p-value
	Internal	TS	Internal	TS	Internal	TS	Internal	TS	
Cirrhosis (F4 vs. F0-3)	87.8 (84.8, 90.7)	88.7 (85.7, 92.2)	86.5 (83.9, 93.9)	88.6 (85.8, 93.2)	79.5 (74.6, 92.6)	78.4 (62.6, 85.8)	2.18	2.16	0.143
Advanced Fibrosis (F3-4 vs. F0-2)	82.5 (78.4, 86.1)	83.9 (79.9, 87.3)	84.2 (79.5, 91.5)	89.8 (85.3, 93.5)	79.5 (67.6, 86.2)	65.1 (58.3, 74.4)	1.73	2.09	0.381
Significant Fibrosis (F2-4 vs. F0-1)	73.9 (69.8, 78.5)	74.8 (70.4, 79.3)	85.2 (74.5, 91.7)	90.6 (77.4, 95)	73.3 (51.1, 80.2)	49.5 (41.6, 69.9)	1.51	2.01	0.221

Table 1 Results of predicting cirrhosis, advanced fibrosis and significant fibrosis using Liver Surface Nodularity (LSN) scores. Area under the receiver operating characteristics curve (AUC), sensitivity, specificity, and LSN cutoffs based on Youden index are shown. 95% confidence intervals are in brackets. The dataset (480 patients) consisted of: F0 stage - 151 patients, F1 stage - 52 patients, F2 stage - 82 patients, F3 stage - 56 patients, and in F4 stage - 139 patients. The p-values were compared using the “roc.test” function from the “pROC” package in RStudio (version 2024.04.2+764). No statistically significant differences were found when comparing the ROC AUCs between the two methods (Internal vs. TS) using a bootstrap test.

Keywords

CT**;** Liver**;** Liver Fibrosis; Cirrhosis; Liver Surface Nodularity