

First-in-human diagnostic study of hepatic steatosis with computed ultrasound tomography in echo mode

Patrick Stähli^{1,4}, Chiara Becchetti^{2,4}, Naiara Korta Martiartu^{1,4}, Annalisa Berzigotti^{2, 3},
Martin Frenz¹, and Michael Jaeger^{1,*}

¹Institute of Applied Physics, University of Bern, Bern, Switzerland.

²Department of Visceral Surgery and Medicine, Inselspital, Bern University Hospital,
University of Bern, Bern, Switzerland.

³Department of Biomedical Research, University of Bern, Bern, Switzerland.

⁴These authors contributed equally.

*email: michael.jaeger@unibe.ch

Content

This supplementary material provides measured CAP values, reconstructed CUTE-SoS images, and extracted liver CUTE-SoS values for each participant. Data acquisition for CUTE-SoS reconstruction was repeated five times; thus, we show all reconstructed CUTE-SoS images and their corresponding liver SoS values. Furthermore, we analyze the sensitivity of the discriminative performance of liver CUTE-SoS estimates to the initial beamforming SoS value and the strength of regularization parameters used in the inversion.

Supplementary Tables

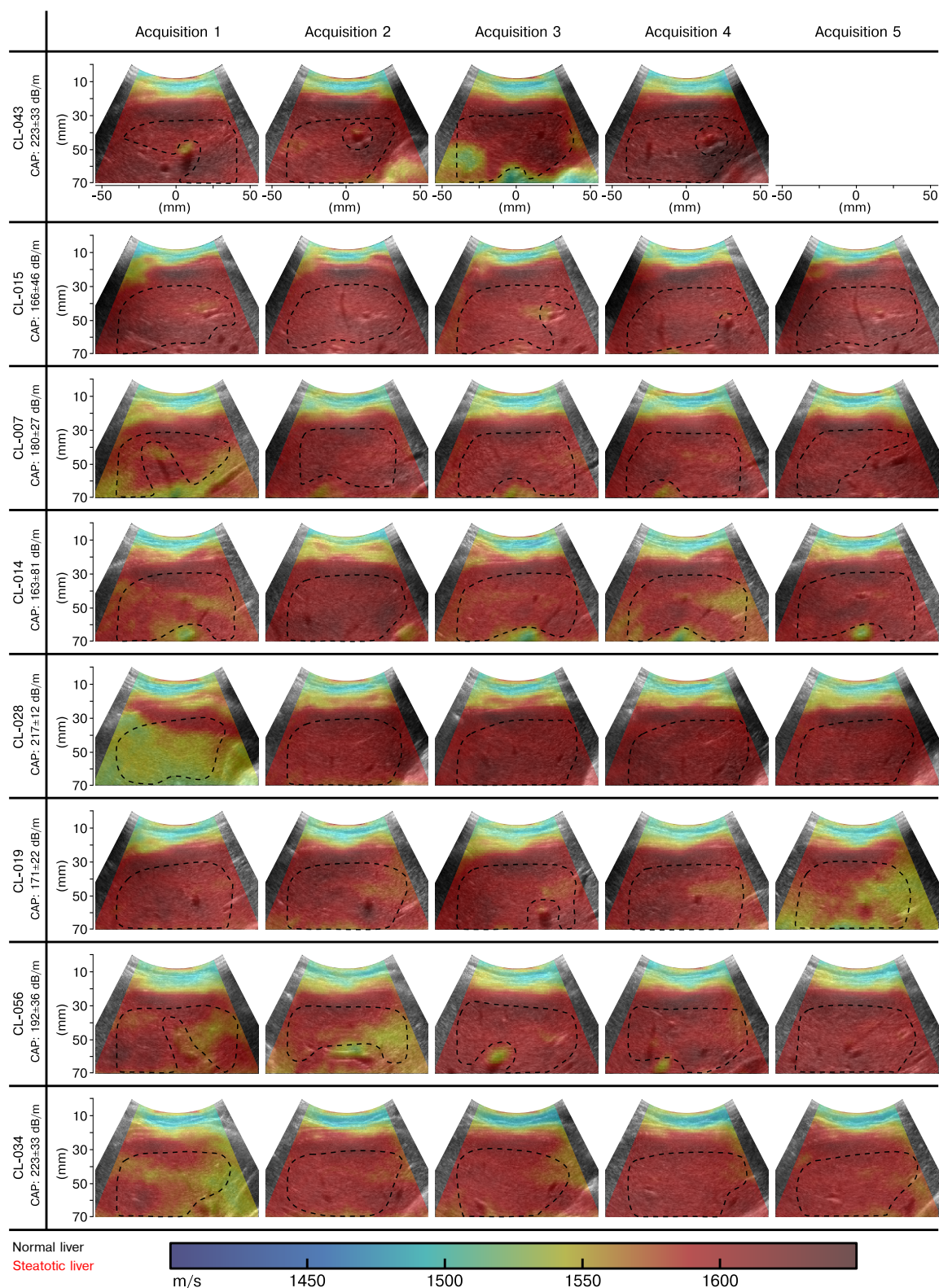
Supplementary Table 1: Data used for statistical analysis in this study. CAP: controlled attenuation parameter; IQR: interquartile range; CUTE: computed ultrasound tomography in echo mode; SoS: speed of sound; SD: standard deviation.

Participant ID	Diagnosis	CAP (IQR) [dB/m]	CUTE-SoS (SD) [m/s]
CL-005	Normal	207 (27)	1567 (12)
CL-007	Normal	180 (27)	1600 (8)
CL-008	Normal	175 (15)	1584 (5)
CL-009	Normal	215 (22)	1551 (11)
CL-010	Normal	162 (21)	1589 (16)
CL-011	Normal	188 (33)	1572 (14)
CL-012	Normal	206 (30)	1568 (3)
CL-013	Normal	229 (30)	1558 (6)
CL-014	Normal	163 (81)	1598 (10)
CL-015	Normal	166 (46)	1606 (9)
CL-016	Normal	226 (18)	1567 (14)
CL-017	Normal	238 (36)	1583 (7)
CL-018	Steatotic	333 (37)	1527 (11)
CL-019	Normal	171 (22)	1595 (11)
CL-020	Steatotic	349 (28)	1556 (9)
CL-021	Normal	200 (48)	1589 (12)
CL-022	Normal	173 (25)	1589 (6)
CL-026	Normal	160 (32)	1575 (11)
CL-027	Normal	233 (10)	1573 (5)
CL-028	Normal	217 (12)	1596 (20)
CL-029	Steatotic	337 (31)	1520 (20)
CL-030	Steatotic	332 (33)	1552 (5)
CL-031	Steatotic	319 (33)	1558 (5)
CL-032	Steatotic	307 (15)	1557 (13)
CL-033	Normal	195 (28)	1587 (4)
CL-034	Normal	175 (60)	1591 (6)
CL-035	Steatotic	312 (40)	1572 (11)
CL-036	Steatotic	355 (42)	1543 (7)
CL-038	Steatotic	338 (44)	1546 (3)
CL-039	Steatotic	394 (14)	1533 (5)
CL-040	Steatotic	283 (11)	1554 (2)
CL-041	Steatotic	331 (15)	1530 (6)
CL-042	Steatotic	347 (30)	1528 (7)
CL-043	Normal	223 (33)	1608 (9)
CL-045	Steatotic	344 (13)	1535 (9)
CL-046	Steatotic	331 (15)	1558 (10)
CL-047	Steatotic	393 (39)	1543 (5)
CL-050	Steatotic	321 (42)	1552 (8)
CL-051	Steatotic	333 (38)	1527 (7)
CL-052	Steatotic	323 (79)	1537 (11)
CL-053	Steatotic	267 (14)	1538 (6)
CL-054	Steatotic	343 (23)	1547 (2)
CL-055	Steatotic	338 (35)	1536 (11)
CL-056	Normal	192 (36)	1595 (9)

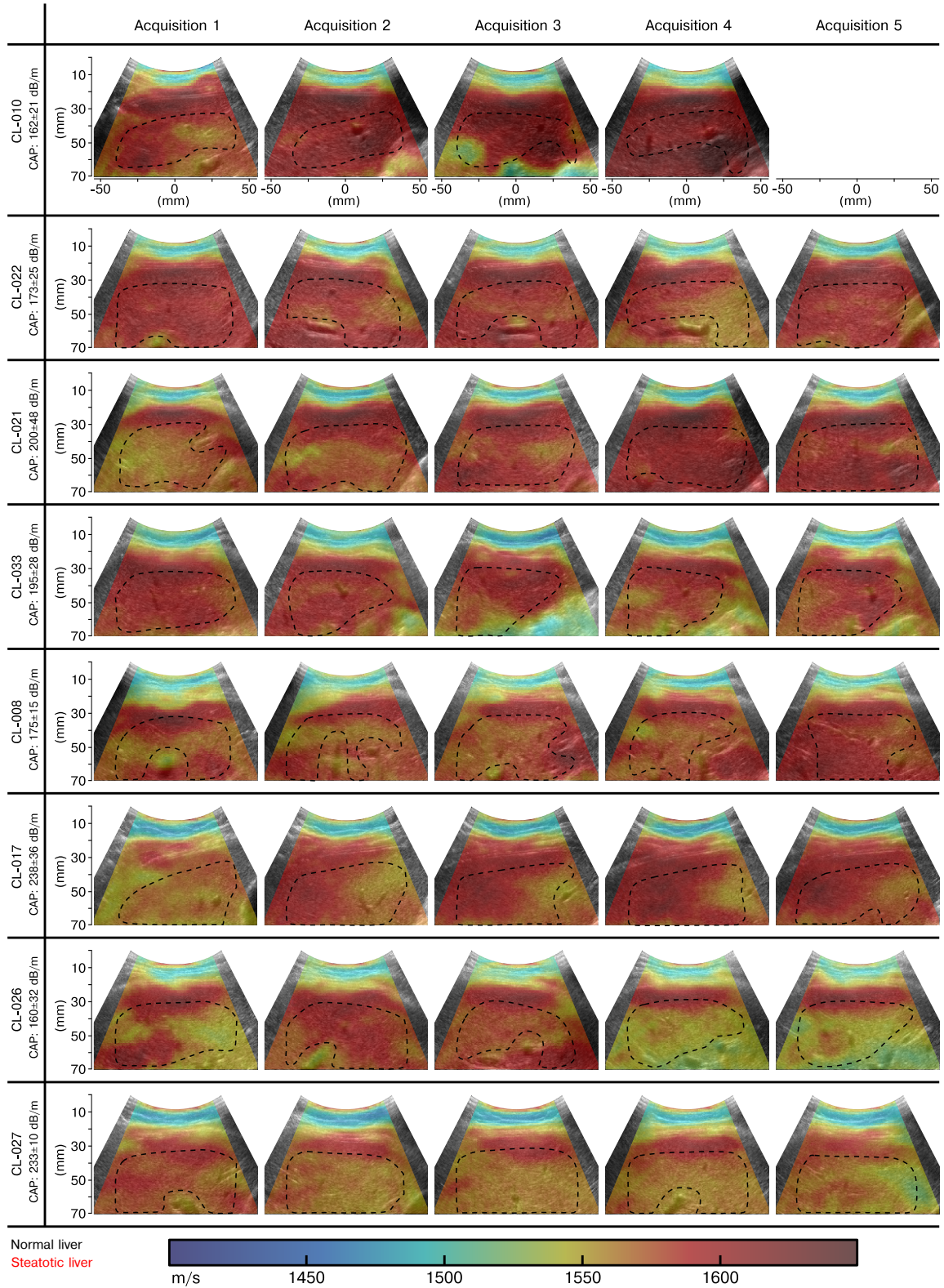
Supplementary Table 2: Mean and standard deviation of liver speed of sound (in m/s) per participant and ultrasound data acquisition (Acq.).

Participant ID	Acq. 1	Acq. 2	Acq. 3	Acq. 4	Acq. 5
CL-005	1574±7	1572±8	1564±7	1546±10	1577±7
CL-007	1587±14	1605±9	1599±10	1600±9	1607±9
CL-008	1583±14	1578±8	1582±10	1580±8	1591±10
CL-009	1539±7	1543±13	1557±18	1565±13	1553±14
CL-010	1586±12	1570±14	1609±11	1591±8	–
CL-011	1554±12	1592±7	1577±8	1575±9	1564±9
CL-012	1566±10	1572±9	1569±7	1568±6	1563±9
CL-013	1560±7	1557±14	1560±14	1547±11	1565±10
CL-014	1589±11	1611±9	1592±8	1590±13	1605±10
CL-015	1606±11	1603±7	1597±7	1604±8	1609±9
CL-016	1555±10	1562±12	1556±10	1581±5	1583±10
CL-017	1571±5	1581±13	1586±14	1591±16	1588±14
CL-018	1528±15	1530±11	1542±8	1514±16	1521±11
CL-019	1600±10	1598±14	1602±12	1600±14	1576±17
CL-020	1544±8	1560±7	1548±9	1561±6	1566±9
CL-021	1573±8	1582±10	1590±12	1602±11	1597±13
CL-022	1595±7	1591±11	1590±9	1579±11	1590±7
CL-026	1577±17	1587±9	1583±9	1564±12	1563±14
CL-027	1581±7	1571±5	1572±7	1572±6	1567±10
CL-028	1561±14	1599±10	1607±7	1610±8	1604±8
CL-029	1497±10	1526±16	1524±15	1549±7	1506±10
CL-030	1557±8	1552±5	1545±6	1548±6	1555±5
CL-031	1562±7	1550±6	1563±9	1555±8	1558±7
CL-032	1535±7	1570±9	1561±10	1558±7	1563±5
CL-033	1592±9	1588±7	1584±18	1582±11	1588±12
CL-034	1580±14	1594±8	1592±8	1597±7	1592±6
CL-035	1556±8	1586±9	1571±6	1576±10	1568±11
CL-036	1542±13	1556±12	1539±9	1540±10	1538±9
CL-038	1546±8	1544±12	1549±12	1543±10	1547±9
CL-039	1537±12	1528±13	1532±11	1530±12	1539±9
CL-040	1554±8	1551±7	1552±6	1555±8	1556±11
CL-041	1525±16	1526±13	1538±14	1530±14	–
CL-042	1529±15	1524±16	1519±8	1539±7	1529±12
CL-043	1608±13	1604±11	1599±22	1620±13	–
CL-045	1548±7	1526±13	1539±7	1528±12	1535±10
CL-046	1545±6	1555±8	1570±9	1554±9	1568±7
CL-047	1538±7	1547±8	1549±8	1541±7	1537±7
CL-050	1552±6	1550±10	1540±10	1563±8	1553±15
CL-051	1532±6	1517±6	1525±4	1533±5	1530±9
CL-052	1548±10	1548±11	1528±8	1536±9	1524±6
CL-053	1542±13	1529±8	1536±5	1546±9	1535±8
CL-054	1547±13	1548±10	1544±15	1546±13	1549±13
CL-055	1537±21	1530±10	1521±14	1547±7	1547±10
CL-056	1590±14	1583±16	1603±9	1602±12	1604±8

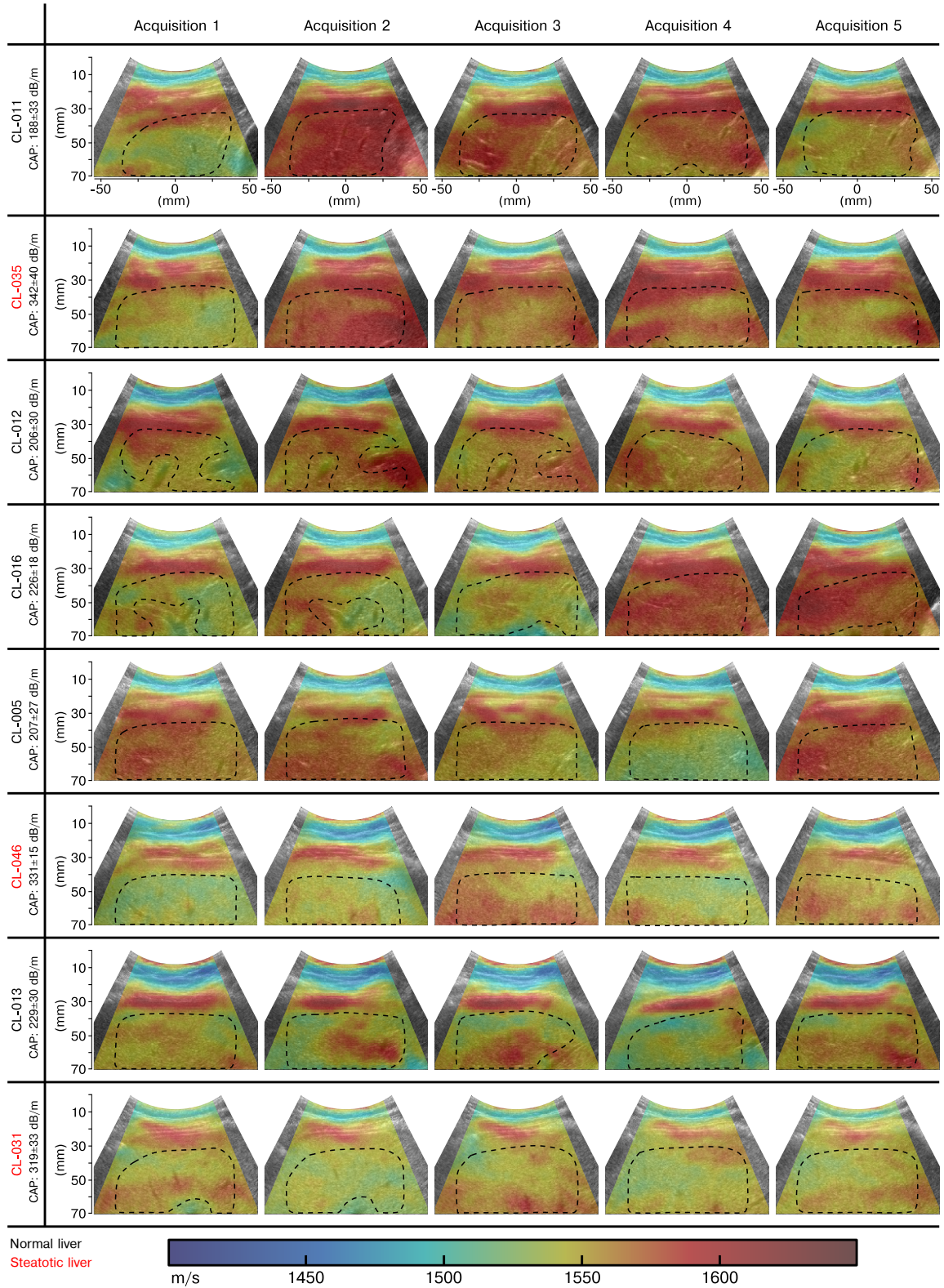
Supplementary Figures



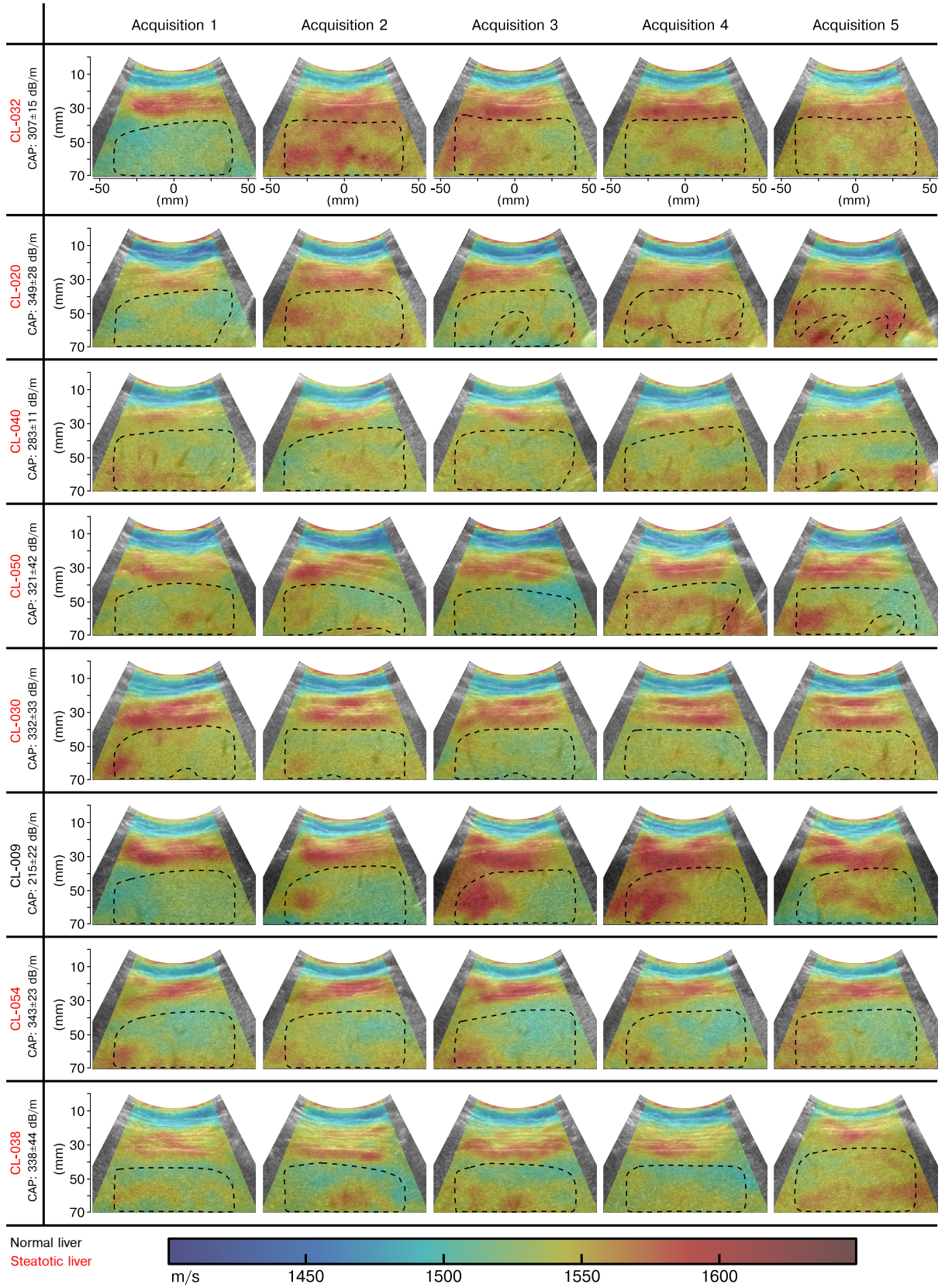
Supplementary Figure 1: Reconstructed speed-of-sound (SoS) images for each participant overlaid on B-mode images. Rows and columns indicate different participants and acquisitions, respectively. Participants appear in descending order in terms of liver SoS values, with the median and interquartile range of controlled attenuation parameter (CAP) values indicated in each case, as well as the diagnostic status. Dashed lines show manually selected regions of interest where mean liver SoS values are calculated. Empty spaces correspond to invalid acquisitions.



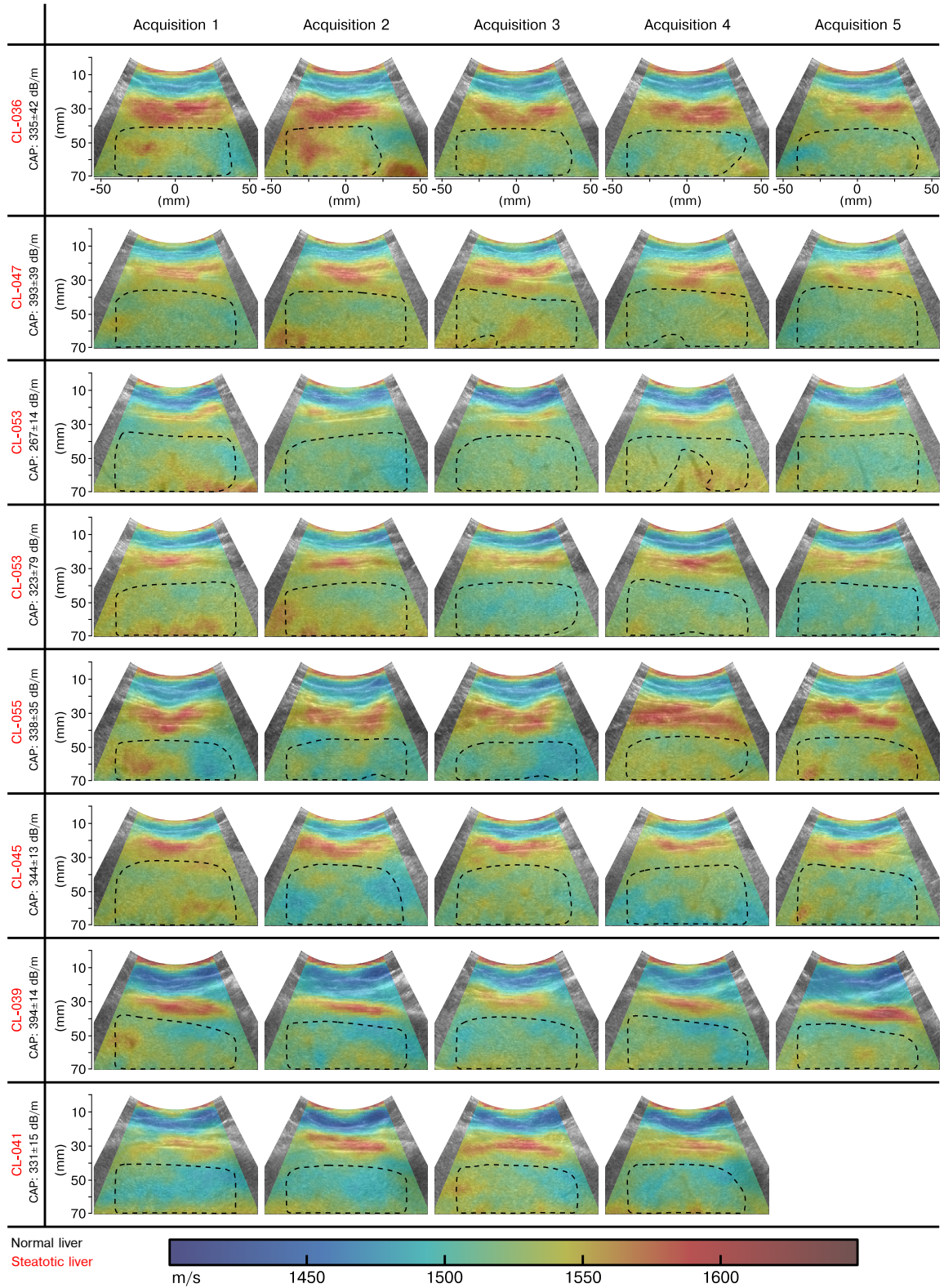
Supplementary Figure 1: (Continued) Reconstructed speed-of-sound (SoS) images for each participant overlaid on B-mode images. Rows and columns indicate different participants and acquisitions, respectively. Participants appear in descending order in terms of liver SoS values, with the median and interquartile range of controlled attenuation parameter (CAP) values indicated in each case, as well as the diagnostic status. Dashed lines show manually selected regions of interest where mean liver SoS values are calculated. Empty spaces correspond to invalid acquisitions.



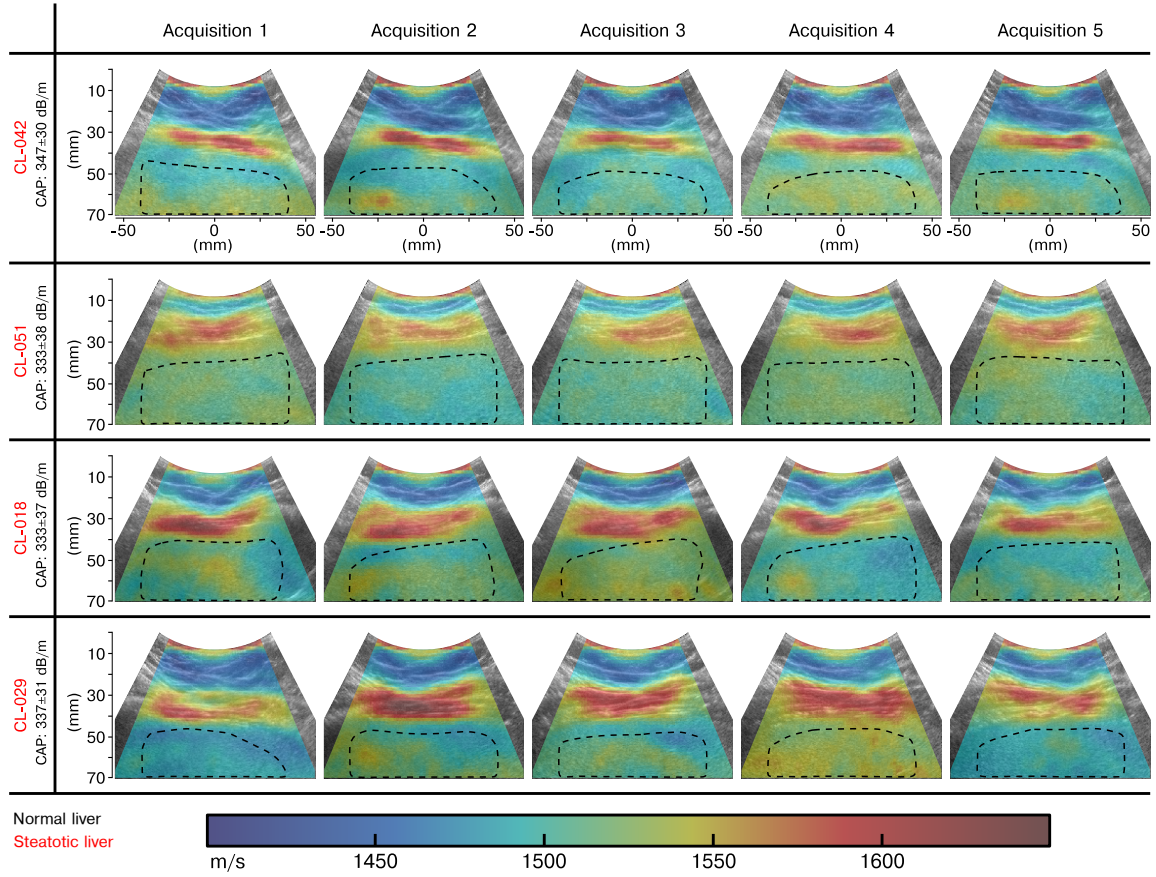
Supplementary Figure 1: (Continued) Reconstructed speed-of-sound (SoS) images for each participant overlaid on B-mode images. Rows and columns indicate different participants and acquisitions, respectively. Participants appear in descending order in terms of liver SoS values, with the median and interquartile range of controlled attenuation parameter (CAP) values indicated in each case, as well as the diagnostic status. Dashed lines show manually selected regions of interest where mean liver SoS values are calculated. Empty spaces correspond to invalid acquisitions.



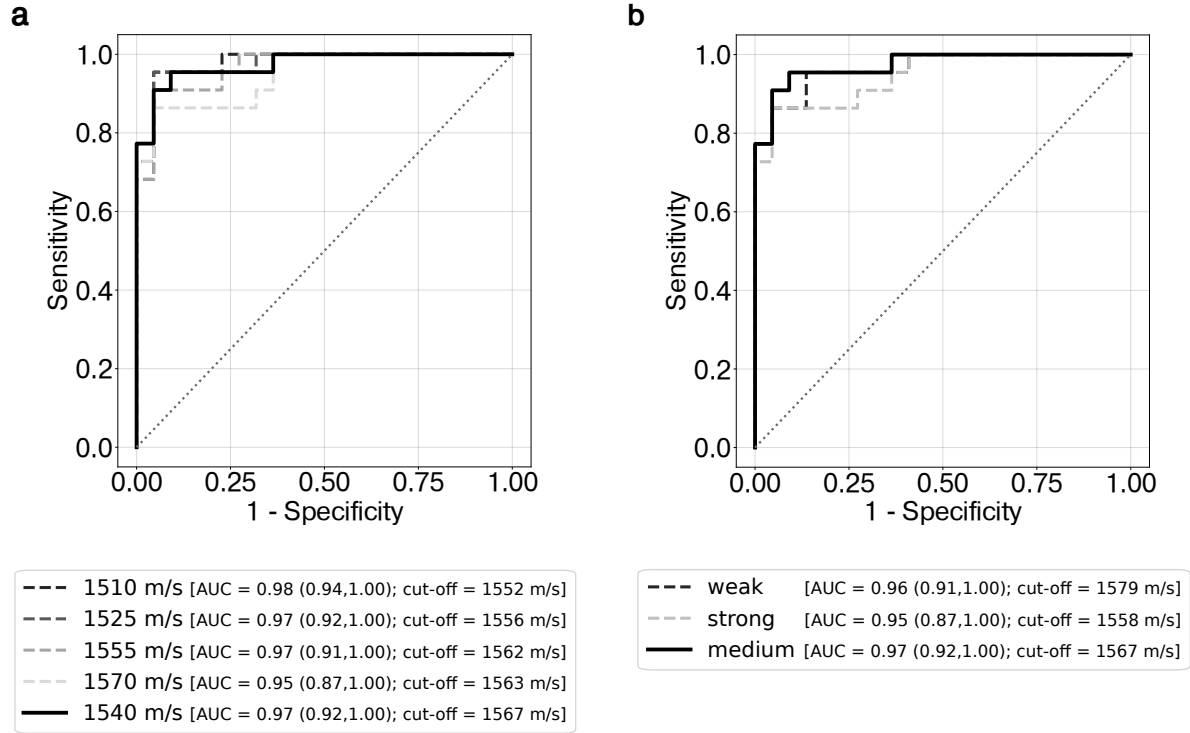
Supplementary Figure 1: (Continued) Reconstructed speed-of-sound (SoS) images for each participant overlaid on B-mode images. Rows and columns indicate different participants and acquisitions, respectively. Participants appear in descending order in terms of liver SoS values, with the median and interquartile range of controlled attenuation parameter (CAP) values indicated in each case, as well as the diagnostic status. Dashed lines show manually selected regions of interest where mean liver SoS values are calculated. Empty spaces correspond to invalid acquisitions.



Supplementary Figure 1: (Continued) Reconstructed speed-of-sound (SoS) images for each participant overlaid on B-mode images. Rows and columns indicate different participants and acquisitions, respectively. Participants appear in descending order in terms of liver SoS values, with the median and interquartile range of controlled attenuation parameter (CAP) values indicated in each case, as well as the diagnostic status. Dashed lines show manually selected regions of interest where mean liver SoS values are calculated. Empty spaces correspond to invalid acquisitions.



Supplementary Figure 1: (Continued) Reconstructed speed-of-sound (SoS) images for each participant overlaid on B-mode images. Rows and columns indicate different participants and acquisitions, respectively. Participants appear in descending order in terms of liver SoS values, with the median and interquartile range of controlled attenuation parameter (CAP) values indicated in each case, as well as the diagnostic status. Dashed lines show manually selected regions of interest where mean liver SoS values are calculated. Empty spaces correspond to invalid acquisitions.



Supplementary Figure 2: Sensitivity of the discriminative performance of liver CUTE-SoS to initial SoS and regularization parameters. **a** Receiver operating characteristic (ROC) curve analysis for liver CUTE-SoS estimates that use initial beamforming SoS values ranging from 1510 m/s to 1570 m/s. The initial SoS value used in the main manuscript is indicated in black. **b** ROC curve analysis for different strengths of regularization parameter values. The results in the main manuscript were obtained with the regularization strength indicated in black (medium). The weak regularization divides by 1.3 the regularization parameter values used in the main manuscript, while the strong regularization multiplies them by 1.4. These factors were chosen to represent the full range of smoothing strengths while maintaining an acceptable trade-off between the spatial resolution and artifact level in CUTE-SoS images. AUC: Area under the curve; cut-off: optimal cut-off liver CUTE-SoS value.