

# Our Metrics

## Understanding cT1

Perspectum Diagnostics provide a comprehensive assessment of liver health based on a range of MRI-derived biomarkers, using our flagship product *LiverMultiScan*<sup>TM</sup>. One of our biomarkers provides a metric relating to inflammation and fibrosis, corrected T1 (cT1).

### What is T1?

T1-relaxation time (measured in milliseconds) is a fundamental parameter in MRI relating to the interaction and energy exchange between the excited hydrogen atoms (usually in water) and the surrounding tissue structure.

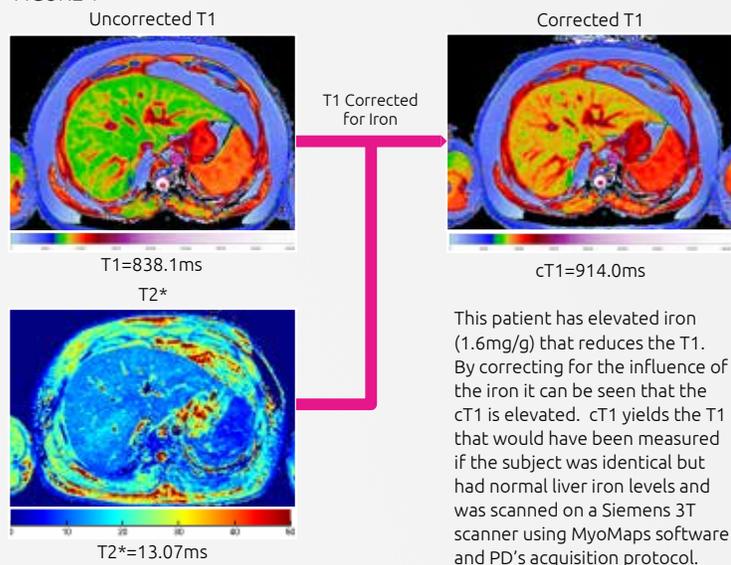
In free fluid, T1-relaxation is relatively long. In healthy tissue, the balance of water and proteins, results in the T1-relaxation being shorter than free water. However, in unhealthy tissue, such as in inflamed and fibrotic tissues, the abundance of free water results in longer T1-relaxation.

### How is T1 corrected?

T2\* is a transverse relaxation time affected by local magnetic susceptibility effects. In the liver, iron deposits, cause inhomogeneities in the magnetic field that have a measurable effect on T2\*<sup>1</sup>.

Iron particles have relaxation properties that affect water and hence reduce T2\*, T2 and the T1. Perspectum uses a patented algorithm that models the effects of iron on the water in the liver and allows the influence of iron to be removed from T1 (see **FIGURE 1**). After removing the influence of excess iron, the resulting measurement is called the corrected T1 (cT1)<sup>2</sup>. Fat has an effect on the cT1 measurement<sup>3</sup>. If the liver tissue does not change in other ways (i.e. changes in inflammation, fibrosis) then an increase in liver fat can, dependant on scanner, cause an increase in the T1 and the cT1 values measured.

FIGURE 1



### Standardization

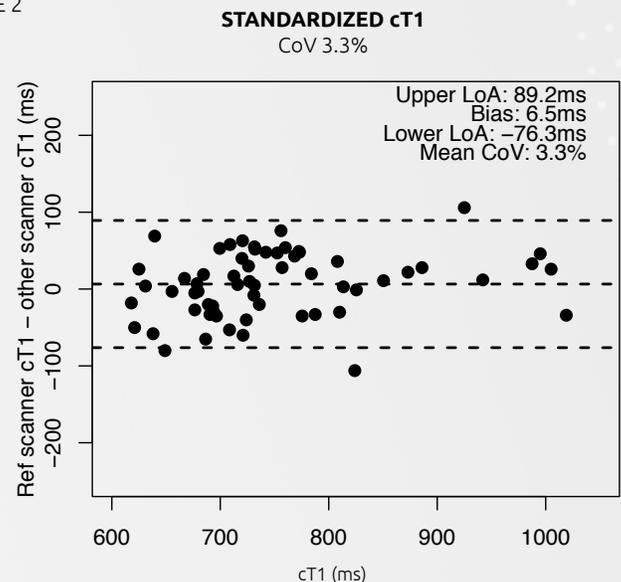
T1 measurements differ depending on magnetic field strength and MR manufacturer. Perspectum Diagnostics standardizes all cT1 measurements to minimize variation and ensure readouts are consistent across MR platforms.

We calibrate between different manufacturers using proprietary phantoms and perform a field strength correction between 1.5T and 3T. Perspectum Diagnostics standardize to the T1 value that would have been measured if that patient had normal iron levels and had been scanned on a Siemens 3T scanner using MyoMaps software. Previously published work refer to pre-standardized cT1 where *LiverMultiScan* had gained regulatory clearance on a single scanner and platform (LMSv1)<sup>6</sup>. In subsequent versions, cT1 values have been standardized across multiple scanners and platforms (LMSv2)<sup>7</sup>. How this relates to our publications is detailed in **TABLES 1** and **2**.

### Corrected T1

Corrected T1 (cT1), as shown in the scan in **FIGURE 2**, is a highly reproducible and repeatable metric that is standardized across MR manufacturers and field strengths<sup>4</sup>. cT1 correlates well with histological markers of pathology<sup>5</sup>.

FIGURE 2



## How does cT1 relate to LIF?

cT1 has also been presented as a Liver Inflammation and Fibrosis (LIF) Score in early publications on LiverMultiScan, to aid clinical interpretation of cT1 values. LIF is a simple mapping of cT1 onto a 0-4 scale, with cut-offs defined based on histological assessment of liver disease.

The derivation of the LIF score is described by Pavlides et al in their 2016 publication. *“Optimal cT1 cut-off points for the differentiation of: no (Ishak fibrosis stage F0), mild (Ishak F1–2), moderate (Ishak F3–4), and severe (Ishak F5–6) fibrosis have been derived from the association of cT1 with histological fibrosis in our previous study. These cut-offs were used to develop the Liver Inflammation and Fibrosis (LIF) score, a standardized continuous score (0–4) which can be derived from many MR systems. For this study, patients were categorized according to LIF score into having: no (LIF <1), mild (LIF 1–1.99), moderate (LIF 2–2.99), or severe (LIF 3–4) liver disease.”*

FIGURE 3

### RELATIONSHIP BETWEEN cT1 AND THE LIF SCORE

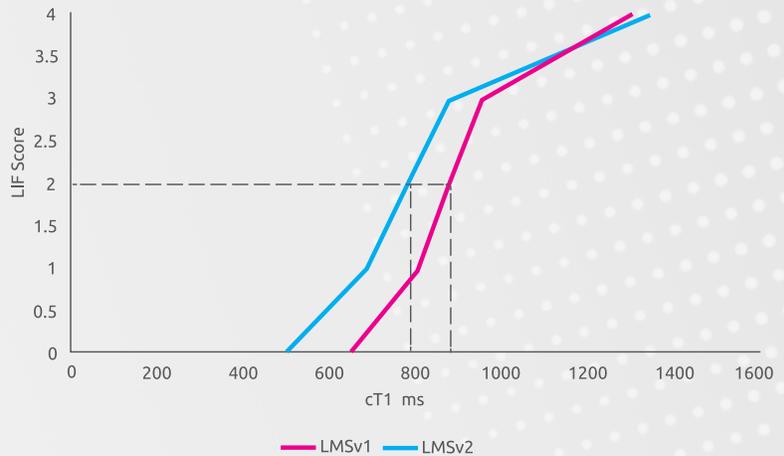


FIGURE 3 shows the relationship between cT1 and LIF for LiverMultiScan device versions

## What does this mean for historic and future LIF and cT1 data?

**FIGURE 3** and the tables below show the relationship between cT1 and LIF. Mapping to standardized cT1 values can also be done retrospectively on already-acquired data and will be reported on all future projects. cT1 is the preferred metric for representing iron-corrected relaxation time of liver tissue and will replace LIF going forward.

Table 1: Publication	LMS Version	LIF	cT1
Banerjee, R., et al (2014). J of Hepatology, 60:69–77.	V1		✓
Pavlides, M., et al (2016). J of Hepatology, 64:308-315.	V1	✓	
Levelt, E., et al (2016). J of the American College of Cardiology, 68:53-63.	V1	✓	✓
Eddowes, P., et al (2017). Alimentary Pharmacology & Therapeutics. 00:1–14	V1		✓
Pavlides, M., et al (2017). Liver International, 1-9.	V1	✓	✓
Harrison, S., et al (2018). Forthcoming.	V1		✓
McDonald., et al (2018). Forthcoming.	V1		✓
Mojtahed, A., et al (2018). Forthcoming.	V2		✓
Bachtiar, V., et al (2018). Forthcoming.	V2		✓

Table 2: Abstract	LMS Version	LIF	cT1
Dennis, A, et al (2018). NASH-TAG, Utah, 4-6 January 2018. Selected Oral Presentation.	V1	✓	
Wilman, H.R., et al (2018). FRI-443. EASL The International Liver Congress, Paris, 11-15 April 2018.	V2		✓
Harrison, S.A., et al (2018). FRI-421. EASL The International Liver Congress, Paris, 11-15 April 2018.	V2		✓
Wilman, H.R., et al (2018). NASH-TAG, Utah, 4-6 January 2018.	V2		✓
Harrison, S.A., et al (2018). NASH-TAG, Utah, 4-6 January 2018. Selected Oral Presentation.	V2		✓

## References

- Wood, J. C., et al (2005) Blood 106(4): 1460–1465
- Banerjee, R., et al (2014) J of Hepatology 60(1): 69–77
- Mozes, F.E., et al (2016) J of MRI, 44(1): 105-111
- Wilman, H.R., et al (2018) FRI-443. EASL The International Liver Congress, Paris, 11-15 April 2018.
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- Perspectum Diagnostics. (2018) Available at: <https://www.prnewswire.com/news-releases/perspectum-diagnostics-announces-fda-clearance-for-livermultiscan-mr-imaging-device-300177120.html> [Accessed 15 May 2018].
- Perspectum Diagnostics (2018) Available at: <https://www.prnewswire.com/news-releases/fda-clearance-for-perspectum-diagnostics-livermultiscan-means-more-patients-can-benefit-from-access-to-state-of-the-art-non-invasive-diagnostic-aid-for-liver-disorders-300561597.html> [Accessed 15 May 2018].