UNIVERSITÀ DEGLI STUDI DI MILANO
DIPARTIMENTO DI FISICA

Multi exponential analysis of the NMR spin-spin relaxation time on healthy and damaged human tissues

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We investigated human tissue samples with proton Nuclear Magnetic Resonance (^{1}H-NMR) with the goal of help physicians to date trauma in cases of physical abuses. We evaluated the spin-lattice T1 and spin-spin T2 relaxation times of the nuclear magnetization at two static fields H=0.2 and 1.5 Tesla. We measured nineteen samples of both healthy and bruised human tissue taken from seven anatomic regions of nine corpses with different skin conformation, to see how their various molecular composition influences the analysis. The data analysis covered both the calculation of experimental errors and the resolution of the multi-exponential decay into a finite number of components, with their relative weights and relaxation times. We studied the statistical deviation's outputs of the regularization method used to solve the inverse Laplace problem. In addition, the multi-exponential components errors and the fit accuracy and sensibility to data fluctuations were taken into account.

NMR

Info on the interaction between the nuclear magnetization and surrounding environment through the relaxation times and absorption spectrum

Probe: ^{1}H is placed in a **static** magnetic field H_0 and **excited** by magnetic RF **pulsed** fields

NMR + ∇H_0 = Magnetic Resonance Imaging (MRI)

Study internals

T_1

$$M_z(t) = M_0\left(1 - e^{-t/T_1}\right)$$

spin-lattice relaxation time:

recovery time towards the thermodynamic equilibrium

T_2

$$M_{xy}(t) = M_{xy}(0)\, e^{-t/T_2}$$

spin-spin relaxation time:

exchange time of energy among spins

$$\text{NMR signal: } S(t) \propto \rho(^1\text{H}) \cdot exp(-t/T_2) \cdot (1 - exp(-t/T_1))$$

Different molecules in human bodies:
- have different contributions in the creation of MRI signal
- vary due to alimentation, diseases, genetics…
- each of them evolves in time
- MRI can distinguish different stages of them in some cases, for instance hemoglobin

Multiexponential signal expected

Our goal: date traumas

Physical Abuse

Some clinical aspects:
- physicians detect it by **excluding** all the other possible **diseases/reasons** of lesions in a **multidisciplinary diagnosis**
- **skin** is one of the most common abused organ
- **bruises** are: among the most prevalent lesions a clinical clue of abuse

Nowadays there is a **symbiotic relationship** between the **dermatological** and **radiological examinations** in the successful detection and diagnosis of inflicted trauma to infants and children.

dating of **injuries helps** physicians to reconstruct the trauma history and to **recognize legal responsibilities** or their lackness.

currently there's **no experimental technique** able to pursue this aim **reliably** and **reproducibly.** [3,4]

Experimental Method

7 anatomic regions — 19 tissue samples — 9 corpses

- III distal part of left forearm, dorsal side
- thorax
- abdomen
- anteromedial left thigh, III distal part
- lateral troncateric region
- parietal region
- tibial plateau

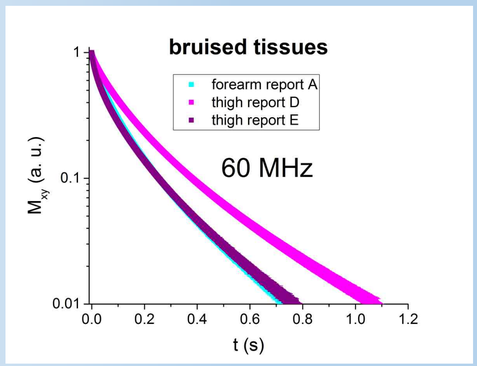
to see how their various molecular composition influences the analysis.

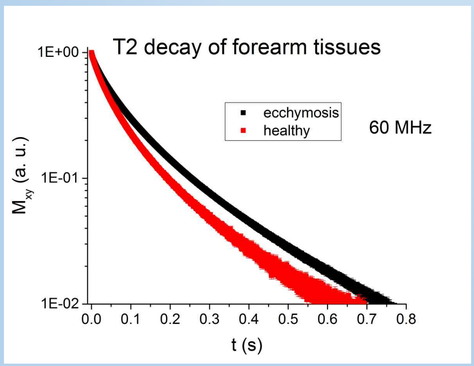
Partial irreproducibility of our data

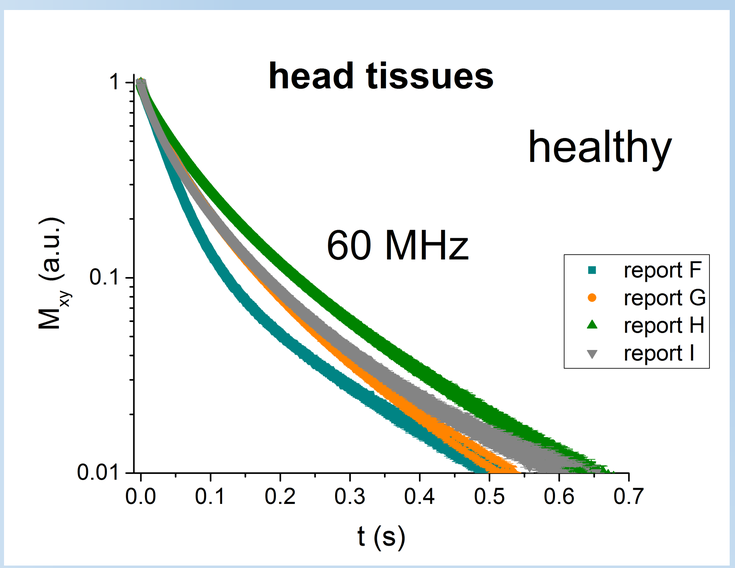
External variables
- Sex
- Ethnicity
- Age
- Post mortem interval
- Cause of death
- Anamnesis

^{1}H nuclei with similar chemical-physical properties, although not equivalent, can be sorted in a finite number of not equivalent molecular groups due to tiny differences.

Experimental measurements





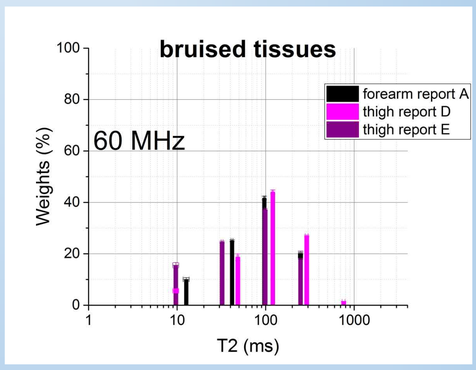


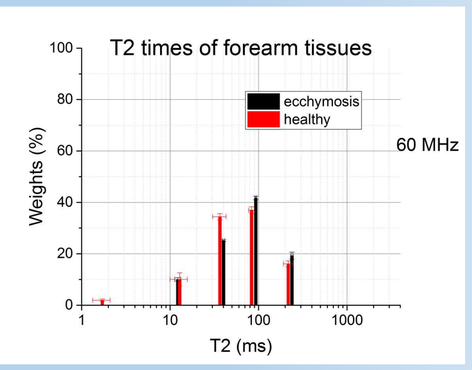
Data analysis method

We got **multiexponential** NMR signal, as we expected, with unknown number, weight and relaxation time of their original components.
We focused on the **T_2** decay curves, and we used a method [2] that solves the **inverse Laplace problem** with a **regularization** technique, Non Negative Least Squares, NNLS [1]. Assumptions on the components of the signal:
- must be in a finite number
- lie between T_{min} and T_{max}
- weights are positive
- are described by δ-functions
- weights are normalized to one

$$y_i = \sum_{j=1}^{M} s_j \exp\left(-t_i/T_{2j}\right) \quad i = 1 \ldots N$$

Data analysis

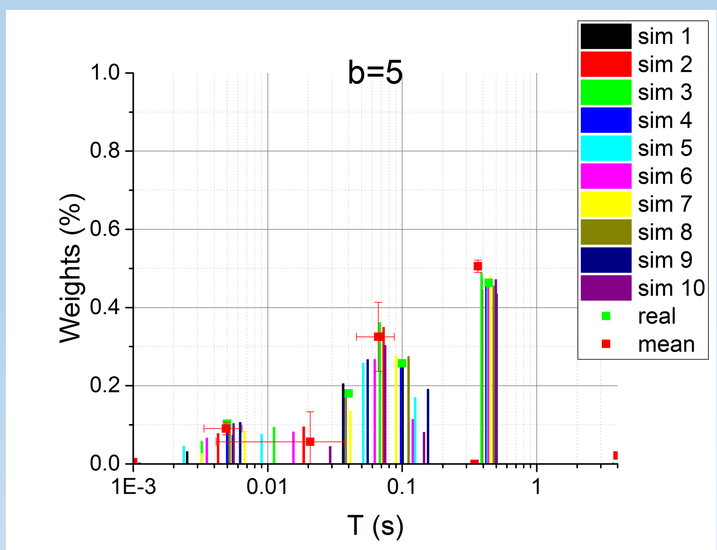


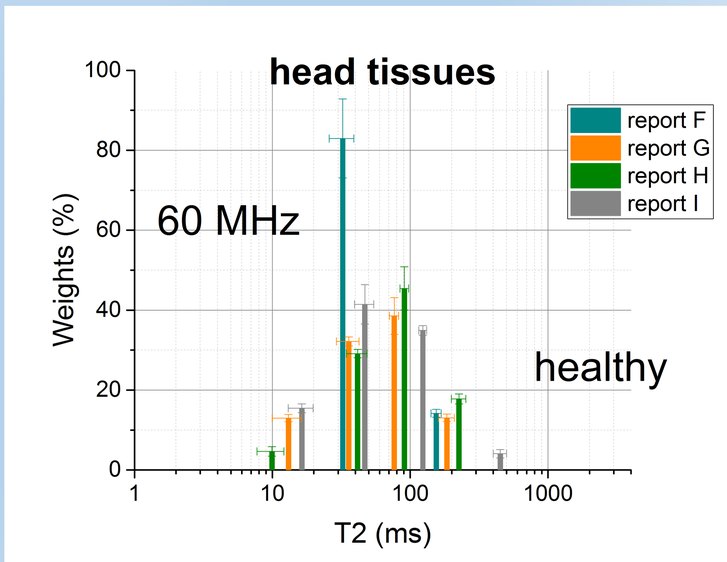


Data analysis method check on simulated data

$$(t_i, \sum_{j=1}^{G} s_j \exp(-t_i/T_j) + c,\ b\sigma_i)$$

$$c : f(c) \equiv N(c, 0, b\sigma_i) = \frac{1}{b\sigma_i\sqrt{2\pi}} \exp\left(-\frac{c^2}{2b^2\sigma_i^2}\right)$$





Conclusions

- Partial irreproducibility of T2 data due to external causes (age, sex, post mortem interval)
- In most cases, we get this T_2 pattern: ~10 ms, 10÷100 ms, ~100 ms, over 100 ms

[1] C. L. Lawson, R. J. Hanson. *Solving least squares problems*. SIAM, 1995.
[2] K. P. Whittall, A. L. MacKay. Jou. Magn. Res. (1969), 84(1):134–152, 1989.
[3] E. M. Hassler et al., Int. Jou. of legal med., 129(2):317–324, 2015
[4] K. R. Nash and D. J. Sheridan, *Jou. Foren. Nurs.*, 5.1 (2009): 31-37.