# NMR STUDY OF THE MALIGNANCY INDEX AND WATER CONTENT IN A TUMOR UTERUS MUSCLE

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$T_1$ and $T_2$ relaxation times in tumor tissues obtained from a uterus muscle have been studied. Calculation of the malignancy index $\Lambda$ has been performed, showing significant differences between the results for normal tissues and pathologically changed ones. No visible correlation between $\Lambda$ values and water content in a tissue has been ascertained.

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## *1. Introduction*

In 1971 Damadian observed that the spin-lattice relaxation times $T_1$ of protons in malignant tumors were generally longer than in case of normal tissues [1, 2]. This led to further researches on both human [3–5] and animal tissues [6, 7] which revealed the same features and confirmed the report made by Damadian. A very similar effect has been observed in the case of spin-spin relaxation time $T_2$ [8, 3].

Koutscher [3] has introduced the concept of malignancy index which is defined as follows:

$$\Lambda = \frac{(T_1)_i}{(T_1)_{\text{normal}}} + \frac{(T_2)_i}{(T_2)_{\text{normal}}},$$

where $(T_{1,2})_i$ is the relaxation time of a given tissue, and $(T_{1,2})_{\text{normal}}$ — the mean relaxation time of normal tissues. The application of the malignancy index has significantly improved the resolution of the method, which resulted in a better elimination of coincidental similarity between $T_1$ and $T_2$ values for normal and pathologically changed tissues [9–12]. Moreover, it has been observed that the malignancy index of a tissue which was collected nearby a tumor also shows a certain deviation from the value for the normal tissue, though its histological diagnosis is the same as for a normal tissue [4, 9].

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In order to explain the reasons why there is a dissimilarity of relaxation times, the following quantities were examined simultaneously, namely:

— tissue water content [7, 9, 13–15]

— tumor growth rate [15, 16]

— histological examination [3, 10, 17]

— the concetration of Na, K, Fe, Zn, Cu, Mn, Co and Ni [2, 9, 18, 19].

In spite of the fact that the mechanism that governs the differentiation of the relaxation time values has not been explained yet, numerous investigations of the application of the NMR method in oncological diagnosis have been undertaken [3, 9, 12].

In this paper some initial results of a systematic study on this subject have been presented.

## *2. Materials and methods*

Cylinder-shaped samples (6 mm high, 5 mm diameter) were obtained from post-operative material from the Institute of Obstetrics and Gynaecology. The material was cooled to 274–277 K within 5 minutes after the operation. These samples were stored for not longer than 48 hours. Both during storage and measurements, tissue samples were carefully protected from drying up.

Measurements were performed on an SXP 4–100 Bruker spectrometer operating at 90 MHz. The spin-lattice relaxation time $T_1$ was measured by the conventional $\pi-\tau-\frac{\pi}{2}$ method. The relaxation time $T_2$ was measured by the application of the Maiboom–Gill sequence. Under the applied conditions of measurement the Fourier transformed free induction decay did not show any evidence of the existence of the resonance line structure, but only its broadening with respect to a sample of pure water. Measurements of $T_1$ and $T_2$ relaxation times were performed at 300 K. When the NMR measurement was over, a part of the sample was preserved in formalin and diagnosed histologically while the rest of the tissue was weighted, dried at 353 K for 24 hours, and reweighted. In this way the water content was determined.

In order to establish the dependence of $T_1$ and $T_2$ on the method of preparation of a tissue sample, the following measurements on 3 kinds of samples were made:

A — a cylinder-shaped sample cut off from the tissue,

B — a cut up tissue,

C — a mechanically squashed tissue.

The process of squashing took place in a metal-homogenizer [20] which was cooled to 275 K.

## *3. Results and discussion*

Figure 1 shows the influence of the mechanical treatment of the tissue on the relaxation time $T_1$. The samples after the mechanical treatment, and especially those which were squashed, have much shorter relaxation times than those of cylinder shape. The results of this experiment explicitly show that in order to avoid the artificial shortening of the $T_1$

value one should take measurements of samples which are not mechanically destructed. Figure 2 shows the influence of the tissue storage conditions on the relaxation time $T_1$. Fragments of myometrium (uterus muscle) and leiomyoma (non-malignant tumor) taken from the same patient were stored both in opened and closed test tubes. As Fig. 2 shows, the relaxation time $T_1$ does not essentially change within 72 hours.

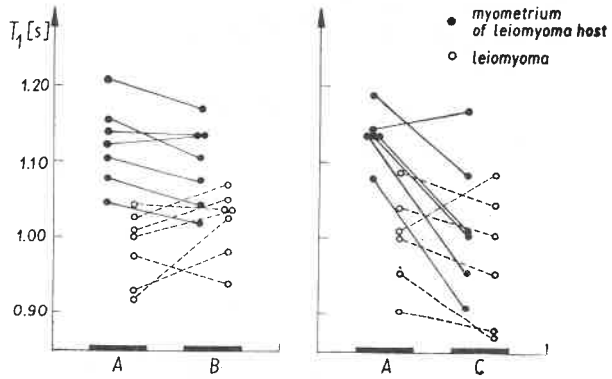


Fig. 1. Influence of the mechanical treatment of samples on $T_1$ values, A — cylinder-shaped tissue samples, B — cut up tissue, C — mechanically squashed tissue

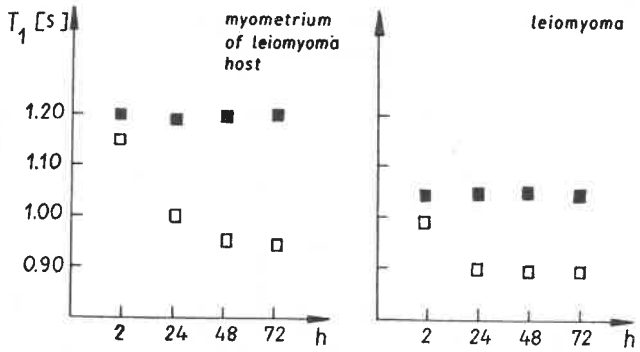


Fig. 2. Influence of time and conditions of storage on $T_1$; ■ — closed test tubes, □ — opened test tubes

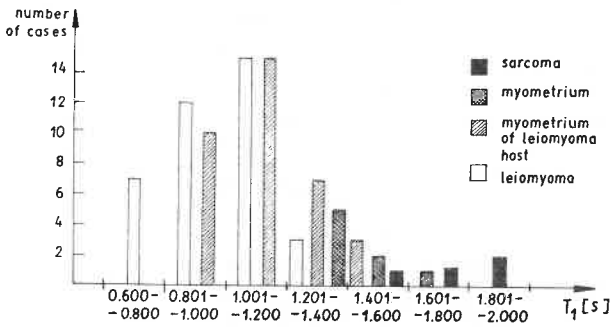


Fig. 3. Spin-lattice relaxation time $T_1$ values for samples of: myometrium, myometrium of leiomyoma host, leiomyoma, sarcoma

The results of measurements of $T_1$ and $T_2$ in the following samples:

— malignant tumor (sarcoma)
— normal uterus muscle (myometrium)
— uterus muscle of a leiomyoma host
— non-malignant tumor (leiomyoma)

versus the number of cases are shown in figures 3 and 4. The values of $T_1$ and $T_2$ in the case of a malignant tumor are longer than in a normal tissue. On the other hand in the case of a non-malignant tumor they are shorter. For tissues taken from the uterus of a leiomyoma host the relaxation times have intermediate values between $T_1$ and $T_2$ compared to normal tissues and leiomyoma.

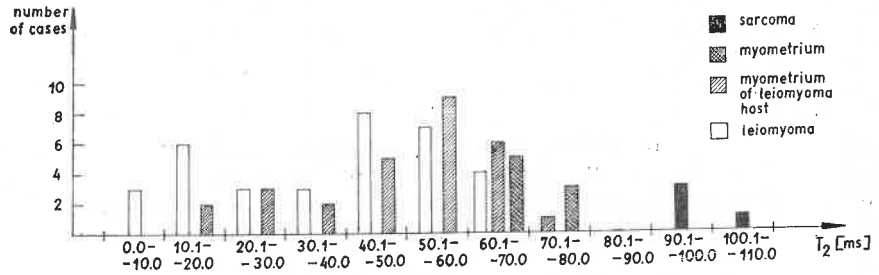


Fig. 4. Spin-spin relaxation time $T_2$ values for samples of: myometrium, myometrium of leiomyoma host, leiomyoma, sarcoma

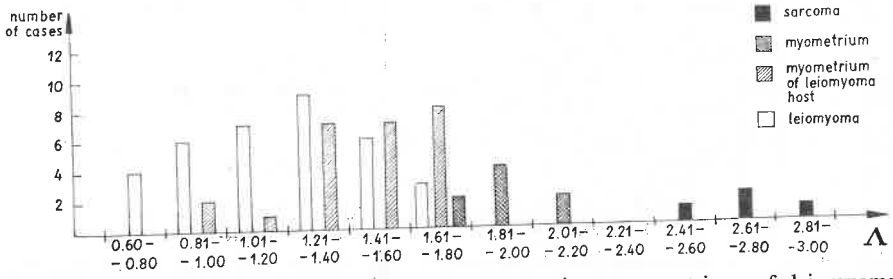


Fig. 5. Malignancy index $A$ values for samples of: myometrium, myometrium of leiomyoma host, leiomyoma, sarcoma

TABLE I

Mean values of: $T_1$, $T_2$ and $A$, $SD$ — standard deviation, $N$ — number of cases

| Tissue | $T_1$ [s] | $SD$ | $T_2$ [ms] | $SD$ | $A$ | $SD$ | $N$ |
|---|---|---|---|---|---|---|---|
| myometrium | 1.365 | 0.142 | 70.3 | 6.4 | 1.917 | 0.114 | 8 |
| myometrium of leiomyoma host | 1.101 | 0.244 | 47.3 | 16.4 | 1.327 | 0.242 | 35 |
| leiomyoma | 0.894 | 0.194 | 38.9 | 17.9 | 1.179 | 0.477 | 38 |
| sarcoma | 1.880 | 0.070 | 99.9 | 9.4 | 2.680 | 0.140 | 4 |

Far better resolution is achieved after calculating the malignancy index $\Lambda$. The results of our measurements and calculations for 88 samples are shown in figure 5. The mean values of $T_1$, $T_2$, $\Lambda$ (Table I) are very similar to those obtained by Fruchter [4].

Among other purposes, our studies were performed to find a correlation between $\Lambda$ (or $T_1$ and $T_2$) and the tissue water content. However, according to our relaxation study, we cannot assume the existence of such a correlation in the range of 75–85% tissue water content (Fig. 6). The difference between the values of malignancy index for normal tissues and for tumor tissues possessing the same content of water is greater than the admissible error of measurement.

Beall [16] and Ranade [14] obtained very similar results for other tissues. The research made by Inch [7], performed within a wide range of a water content, shows that above 50% of the content of tissue water a change over $\pm 5\%$ negligibly affect $T_1$. This convinces us that in this range of water concentration changes of the malignancy index do not depend on the water content in a given tissue.

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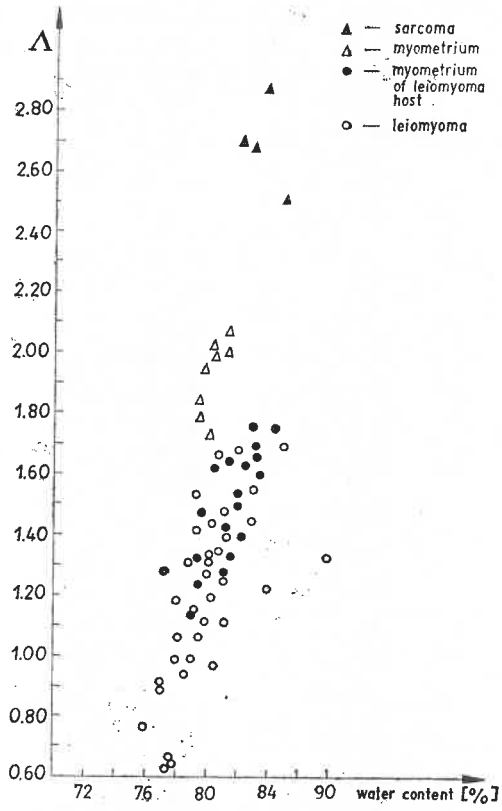


Fig. 6. Water content (%) versus $\Lambda$ for samples of: myometrium, myometrium of leiomyoma host, sarcoma

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