

Quantification of Total Choline in Breast Tumors using syngo GRACE and PRISMA: Initial Experience at 1.5T

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Introduction

Choline is a metabolite that is relatively simple to observe using MR 1H spectroscopy and is recognized as a metabolic marker of active tumor tissue. What is observed with MR Spectroscopy (MRS) is a compound effect of the presence of not only choline but also choline derivatives such as phosphocholine, phosphatidylcholine, glucophosphocholine... Usually, the observed MRS signal is referred as tCho for "total choline".

The mechanisms of the accumulation of choline in cancer cells are not fully understood. Choline together with glucose transport and phosphorylation may be stimulated in breast cancer cells, due to up regulation of choline kinase and transporter genes [1]. It leads to an intracellular accumulation of phosphocholine. This can be observed dynamically using choline labelled with an isotopic marker or statically through measurement of the choline content of tumor. MRS may achieve this measurement noninvasively. Accumulation of choline derivatives is a rapid phenomenon in cancer cells. So, the variation of tissue tCho contents may prove to be a short-term indicator of the level of tumor activity and/or viability. To evaluate choline as a marker of response to treatment, quantification of the metabolite is needed, and has to be repeated with good reproducibility. This raises specific problems in clinical spectroscopy.

We implemented a clinical quantitative technique using the syngo GRACE spectroscopy method, an internal water reference method and PRISMA* for spectroscopy post-processing, to assess the concentration of tCho in breast cancer, and its measurement error. PRISMA* is a PC standalone WIP package (Siemens Medical Solutions, Erlangen, Germany) for spectroscopy post-processing in the time domain. The method is robust, fully automatic and includes quality assessment. We report our initial experience using this protocol for quantitative single voxel ¹H spectroscopy of breast tumors during neo-adjuvant chemotherapy.

*WIP. Works in Progress: This information about this product is preliminary. The product is under development and not commercially available in the U.S., and its future availability cannot be ensured.

Method

For quantification we used an internal reference as described by Meisamy et al. [2] at 4T, where [tCho] is derived from the water molal concentration. Where:

$$f_{T1} = 1 - \exp(-TR/T1) ; f_{T2} = \exp(-TE/T2);$$

η = number of 1H nuclei per molecule (2 for water and 18 for tCho)

MW = molecular weight

A = amplitude of measured signal

The clinical application of this method requires that:

1. All scans have to be acquired from the same voxel, and in the same coil sensitivity condition.
2. The T1 and T2 of tCho may be fixed by reference values obtained on preliminary experiments.
3. The water T2 or A0 (full relaxed amplitude) is measured in each experiment.
4. The correction for water T1 is eliminated by approximating full relaxation condition at TR of 6s for the water unsuppressed acquisitions.
5. The measured tissue water content is assumed to be mono-compartmental and relatively insensitive to change.

The syngo GRACE application for breast spectroscopy offers the capability to perform a single voxel acquisition of a breast lesion in less than 10 minutes.

We did the MRS acquisitions during routine breast MRI examinations also including coronal T2-weighted images, coronal 3D FLASH dynamic series, high-resolution fat-suppressed, MT prepared 3D T1-weighted

$$[tCho] = \frac{10^6}{MW_{water}} \left(\frac{\eta f_{T1} f_{T2}}{A} \right)_{water} \left(\frac{A}{\eta f_{T1} f_{T2}} \right)_{tCho} \quad (\text{mmol/kg})$$

FLASH sequence and targeted diffusion-weighted imaging (DWI) with ADC map [3].

The acquisition scheme was as follows:

Step 1: Localizer reference images

- Using thin MIP reconstruction, the 3D subtraction data set is reformatted into 3 orthogonal plans centered on the lesion;
- these images are stored in a new series and loaded in the exam localizer when opening the MRS protocol.
- Before MRS, a patient positioning scout is acquired in each reference plan.

Step 2: Voxel planning

- The measurement voxel is adjusted to cover the maximum of the contrast-enhanced lesion, with a minimum of adipose tissue inclusion in each plane,
- 6 OVS bands are positioned at the voxel borders.

- For horizontal MRS the last acquisition should be used to facilitate the same repositioning, and voxel size should be readjusted following the above criteria, as the lesion may change with response to therapy.

Step 3: Shim adjustment

- The best result of 2 consecutive auto-shim should be used to improve the FWHM of the water magnitude spectrum to less than 24 Hz using linear shims manually.
- At visual inspection, if the water is less than twice the fat amplitude, the size and/or position of the voxel should be readjusted.

Step 4: tCho acquisition

- The *syngo* GRACE protocol was applied with a TR/TE = 1500/135 ms and NS = 192.

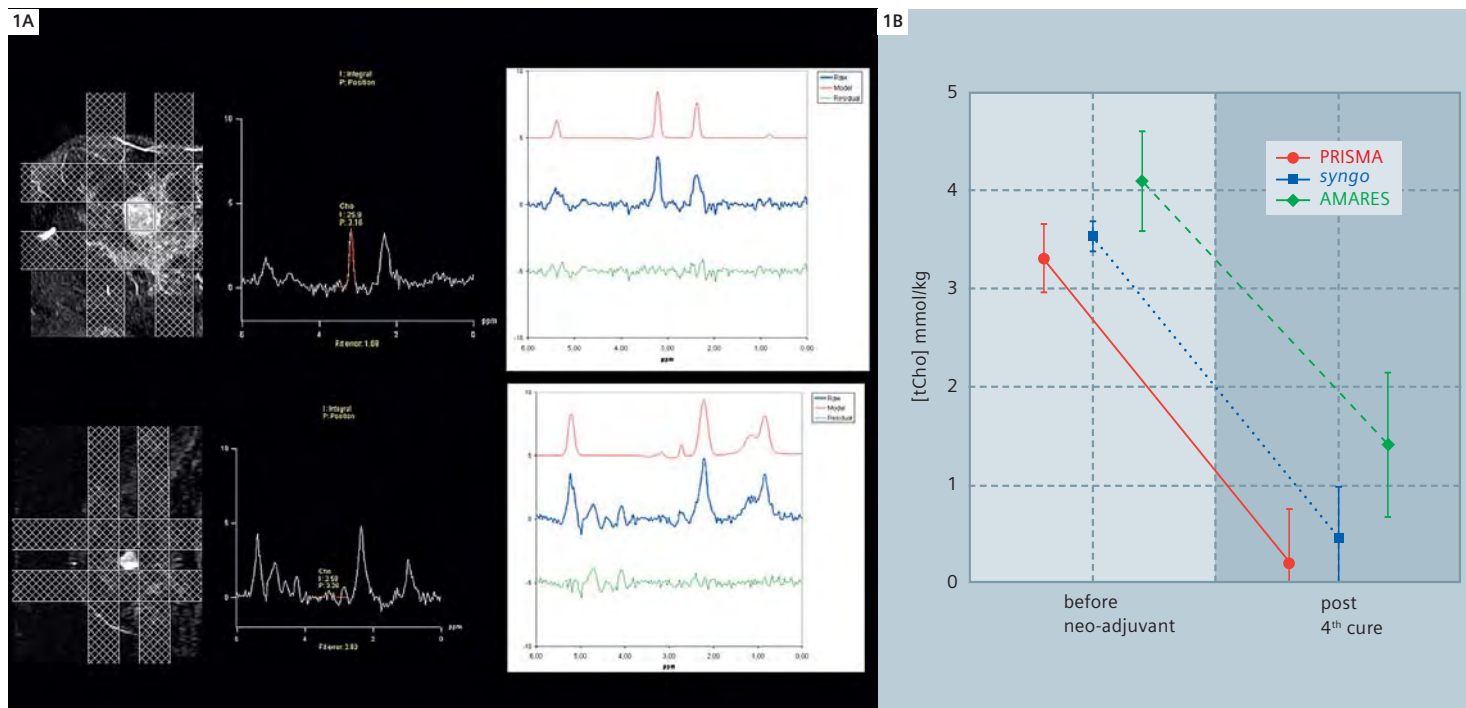
Step 5: tCho and water-reference acquisition

- During tCho acquisition, the same measurement protocol is appended to queue and modified without altering the voxel adjustment, obtaining 5 water-reference scans at different echo time (TE = 50, 75, 100, 125, 150), with water and fat suppression turned off, TR of 6000 ms and 4 repetitions.

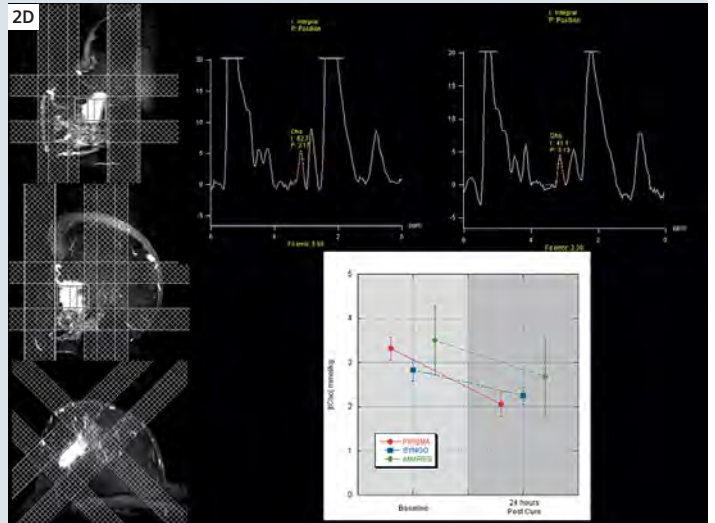
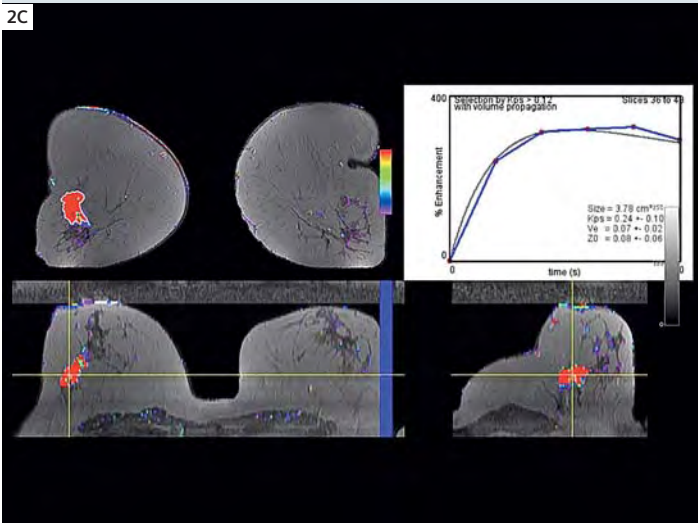
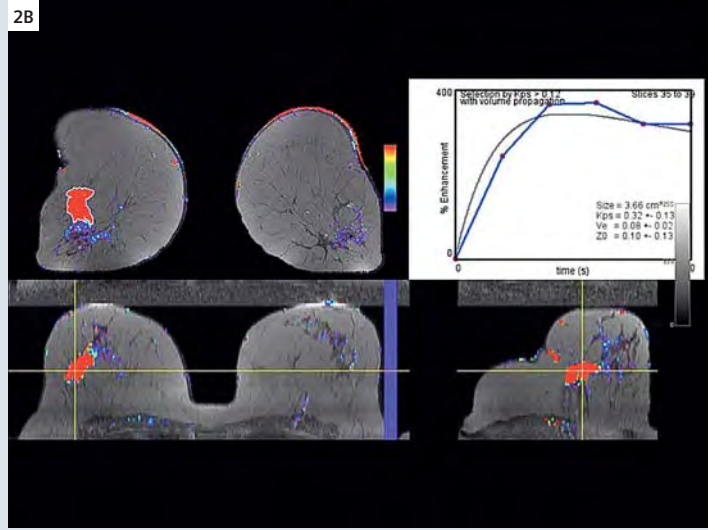
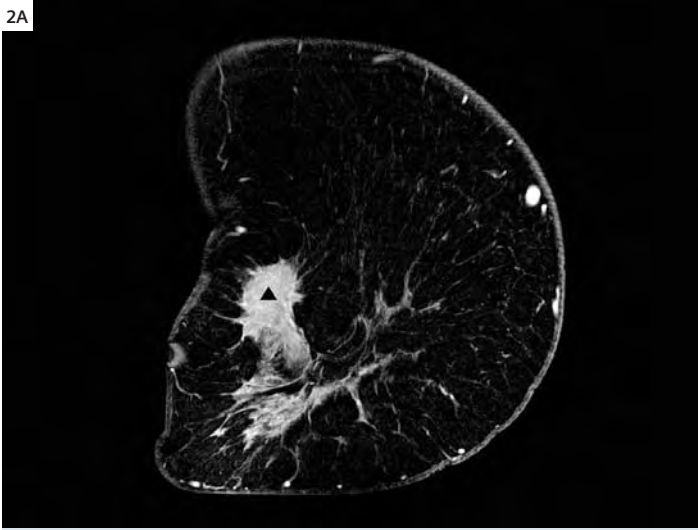
Step 6: Patient position check

- After MRS acquisition, the positioning scout is restarted to check for patient immobility.

Figures 1 and 2 show results in typical patients.



1 47-year-old patient with an invasive ductal carcinoma in the left breast, 4 cm in size, treated with neoadjuvant chemotherapy (Taxotère®). Figure 1A shows the localizer, spectrum and PRISMA output at baseline (upper row) and after 4 courses of chemotherapy (lower row). The size is clearly reduced (1.4 cm) and the sample volume had to be reduced accordingly. The calculated [tCho] at baseline was 2.35 (+ 0.42) mMol/kg. After the end of treatment (4 courses), the Cho peak is in the range of background noise. Figure 1B shows the graph of [tCho] calculated using the PRISMA and two other processing methods (MRUI/AMARES [4] and basic *syngo* processing).



2 41-year-old patient with an invasive ductal carcinoma in the right breast, 3 cm diameter, with no palpable lymphadenopathy. On the baseline MR examination the targeted HR, MTC prepared, fat suppressed T1-weighted FLASH sequence (**Fig. 2A**) shows a mass in the right outer quadrants with a typical, spiculated appearance (black triangle). The DCE-MRI analysis using a pharmacokinetic model (**Fig. 2B**) shows a hypervascularized tumor with a transfer constant (Kps) markedly increased and numerous voxels with a washout phenomenon. 24 hours after the first course of neoadjuvant chemotherapy with FEC (Fluorouracil, Epirubicin, Cyclophosphamide), there is a marked reduction of the Kps values without significant reduction in size (**Fig. 2C**). The spectrum (**Fig. 2D**) shows a clearly visible tCho peak. The calculated [tCho] using PRISMA at baseline was 3.32 (+/- 0.27) mMol/kg. 24 hours after the first FEC course there is a reduced tCho peak with a calculated [tCho] at 2.05 (+/- 0.27) mMol/kg. Figure 2D also shows the graph of [tCho] calculated using the PRISMA and two other processing methods (MRUI/AMARES and basic *syngo* processing).

Conclusion

Our first experience with quantitative single voxel MRS of tCholine in breast tumors using *syngo* GRACE and PRISMA at 1.5T is encouraging regarding both the feasibility in the clinical setting and the ability to show a significant decrease in tCho contents as early as 24 hours after initiation of chemotherapy. Provided that a rigorous method is applied, the technique does not require high field nor special hardware. Quantitative MRS gives an insight into the metabolic changes of tumor tissue and may be less related to microenvironmental changes than the

vascular changes reflected by DCE*-MRI. As such, it may contribute to the definition of new surrogate markers for treatment response assessment. Prospective series are needed to assess the prognostic reliability of this marker.

References and suggested reading

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