Assessment of Radiotherapy Treatment in Cervical Cancer using Proton Magnetic Resonance Spectroscopy at 3 Tesla: a Pilot Study

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Introduction: In vivo proton magnetic resonance spectroscopy (MRS) has proven to be helpful in both the initial diagnosis of cervical carcinoma and the subsequent surveillance after radiation therapy [1]. The characteristic metabolite pattern observed in malignant cervical disease is an elevation of choline signal, while decreasing choline level is representative of a successful treatment response. However, for choline level to aid clinical diagnosis it would be extremely important to determine choline quantitatively. Choline quantification can be limited by poor signal to noise ratio using external receiver coils at 1.5 T. In this study, we performed proton MRS in the invasive cervical squamous cell carcinoma using an external phased array surface coil at 3.0 T to evaluate the potential of choline as a biomarker for assessing treatment response quantitatively.

Methods: Four patients (mean age = 45 ± 7 years) with biopsy-proven cervical cancer (Stage II to IVa) were included in this study. A baseline scan was done prior to the start of radiotherapy. Patients were re-evaluated within a few weeks after completion of the treatment. The examinations were undertaken on a clinical 3.0 T MR system (Achieva 3.0 T, Philips Medical Systems, Best, Netherlands) in combination with a 6-element SENSE cardiac surface coil. The spectral signals were acquired from the element 2 and 5 of the coil to optimize data acquisition. Water-suppressed single-voxel proton MRS (SVS) of the cervical lesion was performed with PRESS localization. A voxel was placed on the same region of the tumor/cervix in pre- and post-therapy measurements on the same patient with less pericervical fat inclusion by an experienced radiologist. Consequently, the voxel size (volume size 6-15 ml) depended on the size of the tumor under examination. Spectroscopic data was obtained with the following parameters: TE 125ms, TR 2000ms, spectral width 2000Hz, sample points 1024, 160 signal averages and 16 phase cycles. T2 corrected unsuppressed water was used as an internal standard and calculated using data from the PRESS sequence of 4 signal averages without water suppression at TEs of 75, 100, 125, 150, 175 [2]. Longer TR (6000ms) was applied on water reference scan to minimize water T1 effect in quantification. Choline signal was quantified as follows: Choline/corrected water = [choline peak area / (water peak area / exp(-TE/T2))$_{water}$] x 10^4 expressed in arbitrary units. All spectroscopy data were analyzed utilizing Advanced viewer software (Philips Medical Systems, Best, Netherlands).

Results: Choline metabolite was detected in all patients before and after the radiotherapy treatment. Figure 1A and 1C show T2-weighted anatomic images from Patient #2 before and after radiotherapy. It can be noted that the cervical tumor (in Fig. 1C) was substantially reduced even disappeared compared to the size in the baseline study (in Fig. 1A). Meanwhile, a significant reduction in choline intensity was also noted (see Fig. 1B and 1D). In every study the choline/corrected water ratio and the largest diameter of tumor were calculated. The results for each patient before and after radiotherapy are summarized in Table 1. The choline /corrected water ratio after radiotherapy was significantly reduced in 3 out of 4 patients (patient #4 is under treatment.).

Conclusion: The preliminary results of our pilot study indicate that pre-treatment choline level can be used as a marker for evaluating treatment response in patients with cervical cancer using external surface coil at 3 T. A larger study is being undertaken to confirm this hypothesis.

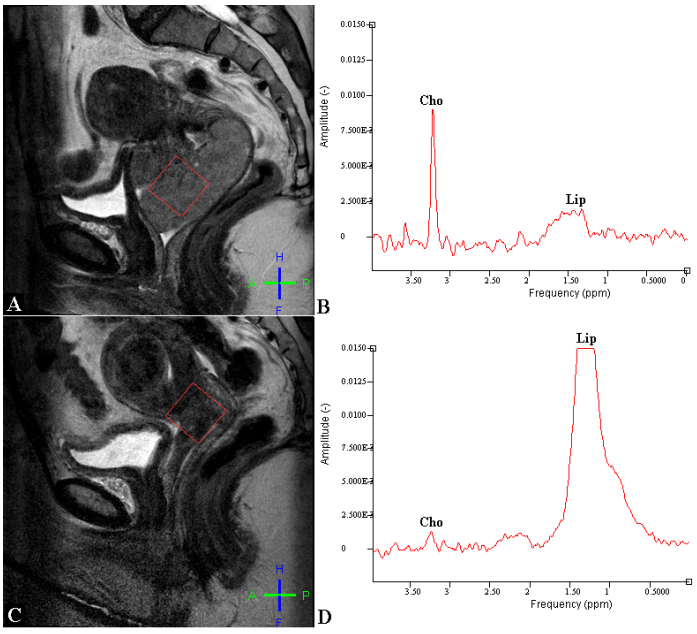

FIGURE 1 In vivo (3T) proton MRS (TR/TE = 2000/125) for evaluation of monitoring treatment of biopsy-proven invasive squamous cell carcinoma of uterine cervix in a 54-year-old woman. **A,** Sagittal non-fat-suppressed T2-weighted image shows a invasive squamous cell carcinoma located at uterine cervix. This image also demonstrates the voxel placement. **B,** Magnified spectrum illustrates a low lipid (Lip) peak, but a high choline (Cho) resonance peak is observed at a frequency of 3.2 ppm. **C,** Sagittal non-fat-suppressed T2-weighted image obtained 3 months later, after completion of treatment with radiotherapy. **D,** There is resolution of the peak centered around choline, which is indicative of local control. The large lipid peak is due to partial volume of the pericervical fat in this region.

Table 1 The Choline/corrected water and tumor size measured in 4 patients before and after radiotherapy.

Patient No.	Choline/corrected water (arbitrary units)		Largest diameter of tumor (cm)		Clinical response
	Pre	Post	Pre	Post	
1	0.89	0.52	4.96	TD	Responder
2	2.3	0.49	8.01	TD	Responder
3	0.78	0.25	4.37	TD	Responder
4	0.69	UT*	6.62	UT*	UT*

TD: Tumor Disappear * Under treatment

References
1. Allen, R. J., *et al., Am J Clin Oncol,* 2001. 24(5): 522-529.
2. Mahon, M. M., *et al., NMR Biomed,* 2004. 17: 1-9.
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