DCE-MRI at 3T in Patients with Advanced Ovarian Cancer Undergoing Neo-Adjuvant Chemotherapy

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Introduction

Ovarian cancer is a genetically heterogeneous disease with a poor prognosis. Its natural history is not well understood, leading to inability to reliably predict treatment outcome. Early identification of patients who do not respond to chemotherapy would allow alternative treatment regimes to be used. Unless the biology of the individual tumours is taken into account individualization of treatment will not be possible. Dynamic Contrast-Enhanced MRI (DCE-MRI) is a technique that can generate parameters thought to reflect the tumour microenvironment such as perfusion and permeability indices (1). The local tumour environment is known to influence treatment response as tumours with reduced perfusion are more likely to be hypoxic and to compromise delivery of chemotherapy (2). This patient group can be challenging to study, due to the extensive disease and intraperitoneal fluid. The aims of this study are to evaluate pre-treatment DCE-MRI parameters in primary and metastatic ovarian cancer, and to assess how these parameters are affected by neo-adjuvant chemotherapy.

Materials/Methods

The study protocol was approved by the Ethics Committee. 16 patients with advanced ovarian cancer (FIGO stage 3 or above) and scheduled to undergo neoadjuvant treatment with chemotherapy prior to interval debulking surgery (IDS) were included in the study. All patients had a staging CT prior to the start of chemotherapy to assess the bulk and location of disease, which allowed the identification of up to three marker lesions: primary ovarian tumour, omental "cake" and peritoneal deposits. DCE imaging was performed before treatment, then repeated after 3 cycles of chemotherapy.

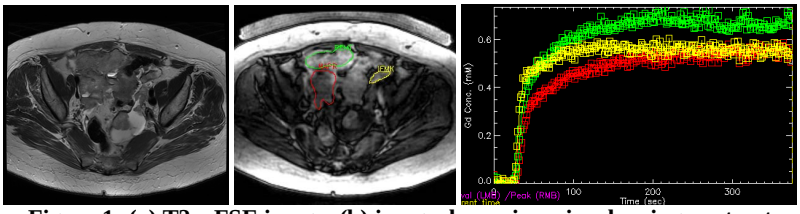

Figure 1: (a) T2w FSE image; (b) image dynamic series showing contrast uptake with ROIs in the primary ovarian mass, omental cake and peritoneal deposit; (c) corresponding curves showing contrast uptake over time.

Imaging protocol: MRI examinations were performed on a 3.0T whole body scanner (HDx, GE Healthcare, Waukesha, WI) using an 8-channel cardiac array coil and a dielectric pad. High resolution axial T2W FRFSE and SSFP images were used to evaluate the extent of the disease and confirm the position of the marker lesions. T_1 mapping was performed using a modified 3D IR-FGRE sequence with multiple inversion times. The dynamic sequence consisted of an axial 3D fast spoiled gradient echo (TR/TE = 2.9/1.3 ms, FA = 18°, FOV = 40×30 cm, matrix 176×132, 20 slices (interpolated to 5 mm thickness), 0.75 NEX, ASSET factor 2) for a total of 7 minutes with a temporal resolution of 1.6 sec. In some patients the PE FOV and matrix were increased leading to a slightly reduced temporal resolution. A bolus injection of Gadobutrol (Gadovist, Schering AG) was given (dose 0.1 mmol/kg at 4 ml/s) followed by a 25 ml saline flush.

DCE-MRI analysis: The three marker lesions were outlined in Cinetools (GE Healthcare, Waukesha WI) by an experienced radiologist on the dynamic images (if present in the imaging volume covered) using the FRFSE and FIESTA images for guidance. Pharmacokinetic analysis of the DCE-MRI images was carried out using custom software written in Matlab (Mathworks, MA, USA). The [Gd] data were fitted with an extended Kety model (3) to allow investigation of the volume transfer constant (K^{trans}) and the rate constant (k_{ep}), as well as the integrated area under the [Gd] curve to 90s (IAUGC90). The modelled arterial input function was based on data from Fritz-Hansen (4), concatenated with the Weinmann curve (5), with the arrival time automatically selected to give the best fit. The Wilcoxon signed rank test was used for statistical analysis of paired comparisons.

Results

DCE data were acquired from 16 patients before treatment and from 14 after three cycles of chemotherapy. Figure 1 shows example images and uptake curves and Table 1 shows the DCE parameters before and after treatment. There was no significant difference in the pre-treatment DCE parameters between primary and metastatic disease. After chemotherapy, there was a reduction in k_{ep} for the peritoneal deposits and a significant reduction for the primary ovarian lesions (p=0.041) but there was no change for the omental cake. This is reflected by a significant difference in the post-treatment k_{ep} between ovarian lesions and the omental cake (p=0.047). There were no significant differences for K^{trans} or IAUGC90.

Discussion & Conclusions

To our knowledge, this is the first study to assess changes in the DCE parameters of primary and metastatic ovarian lesions following neo-adjuvant chemotherapy in patients with advanced ovarian cancer. Our initial results in a small population demonstrate site-specific changes in k_{ep} as a result of treatment. These may reflect the mixed treatment response that often occurs clinically at different disease sites and may be related to variations in blood supply, which can influence the efficacy of chemotherapy. This may also explain the overall pattern of tumour recurrence in this group of patients. Further work, in this ongoing study, will include correlation with tumour response to treatment using RECIST criteria, sequential CA-125 measurements and progression-free survival data.

	Tumour	N	Pre-chemo	Post-chemo	Change	p-value
K^{trans}	Ovarian	14	0.11±0.05	0.12±0.05	0.01±0.04	0.397
	Omental	9	0.12±0.06	0.13 ± 0.08	0.01±0.06	0.859
	Peritoneal	7	0.12±0.04	0.11±0.06	-0.01±0.07	1.000
k_{ep}	Ovarian	14	0.36±0.11	0.29±0.10	**0.07±0.12**	**0.041**
	Omental	9	0.41±0.13	0.42±0.09	0.04± 0.09	0.678
	Peritoneal	7	0.43±0.08	0.34±0.12	0.03±0.20	0.063
IAUGC90	Ovarian	14	15.4±7.6	17.1±6.9	1.7±5.6	0.300
	Omental	9	16.0±8.1	17.2±9.4	1.1±7.4	0.859
	Peritoneal	7	17.3± 6.5	16.0±8.0	-1.2±10.1	0.866

Table 1: DCE parameters before and after treatment (mean ± SD).

References

1. Leach MO et al. Br J Cancer 92:1599 (2005). 2. Padhani AR et al. Abdom Imaging 30:324 (2005). 3. Tofts PS et al. JMRI 7:91 (1997).
4. Fritz-Hansen et al. MRM 36:225 (1996). 5. Weinmann HJ et al. Physiol Chem Phys Med NMR 16:167 (1984).

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