THERAPEUTIC RESPONSE ASSESSMENT USING DYNAMIC CONTRAST-ENHANCED MR IMAGING IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA: AN INITIAL STUDY AT 3T

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Introduction

Metastatic medullary thyroid carcinoma (MTC) is the one of the best characterized solid tumors in regard to its pathologic, biochemical and molecular genetic properties. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has been shown to be capable of evaluating microcirculation and angiogenic properties of various tumor entities [1], and has been considered to be a predictive marker to evaluate thyroid tumor treatment response [2]. MRI is especially important to play a complementary role in monitoring long-term follow-ups of MTC patients [3]. So far, the majority of DCE-MRI studies of thyroid carcinoma have been performed at 1.5 T. We performed for the first time DCE-MRI of MTC a trail at 3T. To the aim of the study was to investigate the changes in microcirculation of metastatic medullary thyroid carcinoma during a long-term antiangiogenic therapy.

Materials and Methods

This study was designed within an interdisciplinary team and was an IRB approved human study. 11 patients with histology confirmed metastatic medullary thyroid carcinomas (MTC), 9 males and 2 females with an average age of 61±15 years, were enrolled in this Phase II clinical trial of a RAF/VEGF-R kinas inhibitor. Patients underwent DCE-MRI using a Gd-chelate (Omniscan, GE Healthcare, 0.1 mmol/kg Bw) with a flow rate of 0.6 ml/s injected after first five repetitions by a power injector (Spectris®, MedRad, Indianola, PA). One baseline scan was performed prior to treatment and follow up scans were scheduled after every 8 weeks of therapy. Dynamic MRI scans were performed on a clinical 3T MR-scanner (Achieva, Philips, Cleveland, OH) using a 3D RF-spoiled fast field echo (3D-FFE) sequence (TR/TE: 8/4ms; FA: 20º; FoV: 250mm; matrix: 256×256; in-plane resolution: 0.98 x 0.98mm^2; slice thickness: 5mm; 20 contiguous slices; acquisition time: 6.7s; 70 time points) with a 2-channel surface SENSE coil.

DCE-MRI data analysis was performed using in-house developed software IDL-based (ITT Inc., Boulder, CO) environment. Signal enhancement within the region of interest (ROI) was evaluated using a two-compartment model, which characterizes the angiogenic and microcirculatory properties of the lesion, and enables quantification of the pharmacokinetic parameters: volume transfer constant (K^{trans}[min^{-1}]) and exchange rate (k_{ep}[min^{-1}]) [4]. Arterial input function (AIF) decomposed k_{ep_adj} [min^{-1}] and k_{pe_adj} [min^{-1}] from an adjusted Brix's model [5]. Color-coded parametric maps (Fig 1) were created as a readily readable, intuitive way of displaying spatial distribution of pharmacokinetic parameters. The results were correlated with biomarkers, such as serum calcitonin level and tumor diameter.

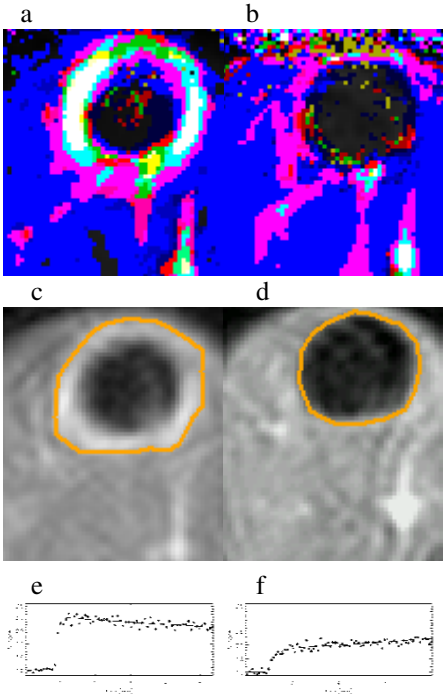

Fig 1, Color-coded DCE-MRI parameter maps of signal-amplitude and k_{ep} pre- (a) and post-therapy (b) of a liver metastasis of a MTC patient. Pre- (c) and post-treatment (d) images show the metastasis with the region of interest (ROI). Signal intensity curves within the tumor ROI from pre- (e) and post-therapy (f) are plotted.

Results

DCE-MRI was successfully performed and quantified in all 25 exams. Characteristic contrast enhancement was observed in the malignant lesion, the artery and benign non-vascular tissue. In total, 25 target lesions from 11 patients were evaluated to monitor the treatment. In 9 of 11 patients follow-up scans after the first treatment revealed significant decrease of K^{trans} , k_{ep}, k_{ep_adj} and k_{pe_adj} ($p<0.01$)with an average decrease of -47%, -37%, -36% and -21% , respectively. Two patients had increased follow-up values in pharmacokinetic parameters, which also revealed readily either increased calcitonin level or increased tumor diameter.

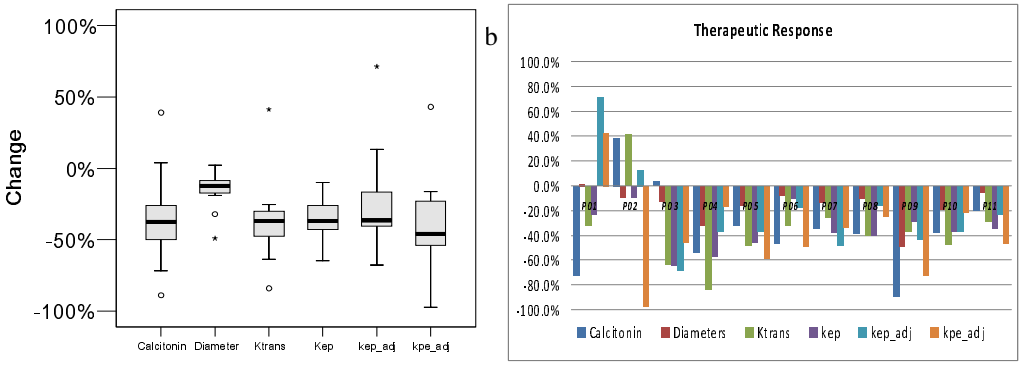

Fig 2, Relative changes of tumor calcitonin level, diameter and DCE-MRI pharmacokinetic parameters between the baseline and the first follow-up scan for all of 25 target lesions (a) and every patient individually (b).

Discussion and Conclusion

This study demonstrated the feasibility of 3T DCE-MRI to assess the microcirculation in metastatic thyroid carcinoma and its changes during therapy. The increased SNR at 3T improves delineation of thyroid carcinoma from surrounding tissue and to determine pharmacokinetics to monitor the biological response of MTC. This indicates that this approach appears feasible for clinical drug development and validation as an imaging biomarker.

References

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