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Comparison between perfusion computed tomography and dynamic contrast-enhanced magnetic resonance imaging in assessing glioblastoma microvasculature

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ABSTRACT

Purpose: Perfusion computed tomography (PCT) and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) provide independent measurements of biomarkers related to tumor perfusion. The aim of this study was to compare the two techniques in assessing glioblastoma microvasculature.
Materials and methods: Twenty-five patients diagnosed with glioblastoma (14 males and 11 females; 51 ± 11 years old, ranging from 33 to 70 years) were includede in this prospective study. All patients underwent both PCT and DCE-MRI. Imaging was performed on a 256-slice CT scanner and a 3-T MRI system. PCT yielded permeability surface-area product (*PS*) using deconvolution physiological models; meanwhile, DCE-MRI determined volume transfer constant (K^{trans}) using the Tofts-Kermode compartment model. All cases were submitted to surgical intervention, and CD105-microvascular density (CD105-MVD) was measured in each glioblastoma specimen. Then, Spearman's correlation coefficients and Bland-Altman plots were obtained for *PS*, K^{trans} and CD105-MVD. $P < 0.05$ was considered statistically significant.
Results: Tumor *PS* and K^{trans} values were correlated with CD105-MVD ($r = 0.644$, $P < 0.001$; $r = 0.683$, $P < 0.001$). In addition, *PS* was correlated with K^{trans} in glioblastoma ($r = 0.931$, $P < 0.001$). Finally, Bland-Altman plots showed no significant differences between *PS* and K^{trans} ($P = 0.063$).
Conclusion: PCT and DCE-MRI measurements of glioblastoma perfusion biomarkers have similar results, suggesting that both techniques may have comparable utility. Therefore, PCT may serve as an alternative modality to DCE-MRI for the *in vivo* evaluation of glioblastoma microvasculature.

1. Introduction

Microvascular proliferation is a crucial histological feature of glioblastoma. Perfusion computed tomography (PCT) and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) are clinical imaging techniques that noninvasively assess the microvascular status of glioblastoma [1–4]. Both PCT and DCE-MRI depend on the dynamic assessment of tracer uptake kinetics, which is subsequently quantified by means of pharmacokinetic models [5,6]. However, PCT and DCE-MRI have specific and respective differences, advantages and drawbacks. Thus, the question arises as to whether perfusion parameters acquired using both methods are comparable. This study aimed to compare the diagnostic performances of pharmacokinetic parameters derived from PCT and DCE-MRI in characterizing glioblastoma microvasculature.

2. Materials and methods

2.1. Patient selection and pathological diagnosis

Informed consent was obtained from each subject; this study was approved by the institutional review board. Thirty patients with suspected high-grade glioma underwent PCT and DCE-MRI preoperatively. No patients received any other form of treatment at the time of imaging or before surgery. The diagnosis was car-

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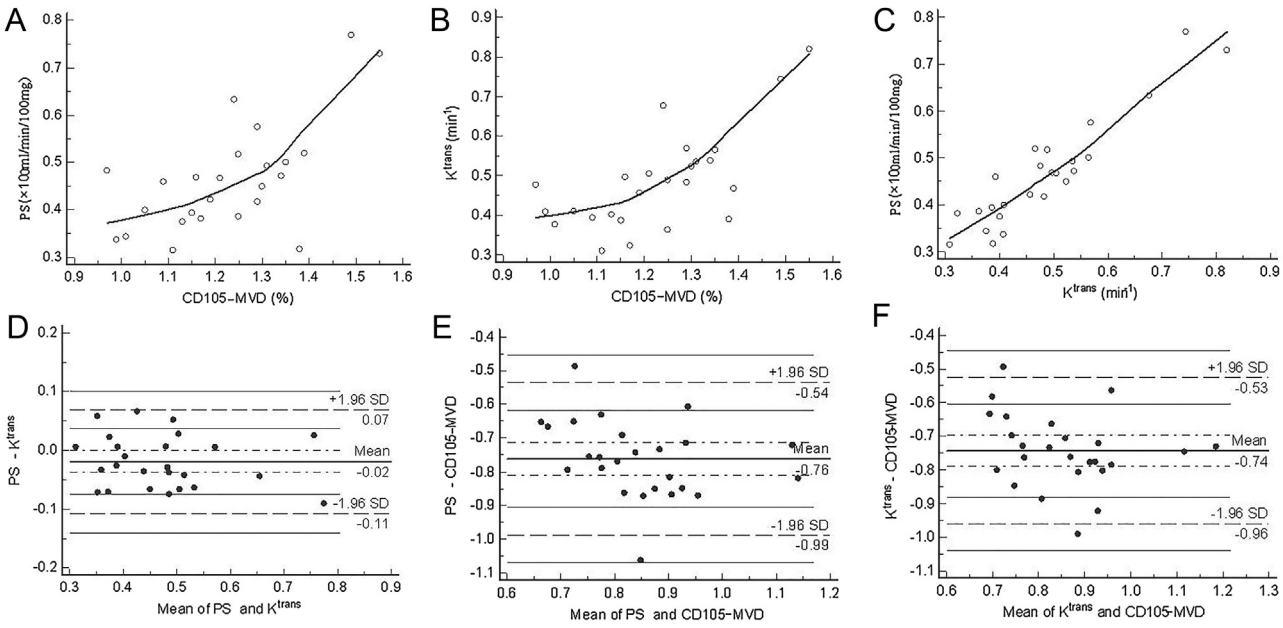

Fig. 1. Graphs showed significant *PS* and K^{trans} correlations with CD105-MVD in glioblastomas (A and B). *PS* was also correlated with K^{trans} in glioblastomas (C). Bland-Altman plots showed no significant differences between *PS* and K^{trans} in glioblastomas (D). There were significant differences between *PS* and CD105-MVD and K^{trans} and CD105-MVD in Bland-Altman plots (E and F). *PS*, highest value of permeability surface-area product; K^{trans}, highest value of volume transfer constant per minute.

ried out according to the 2016 World Health Organization (WHO) classification [7]. Pathological evaluation revealed 25 with glioblastoma. They included 14 males and 11 females, aged 51 ± 11 years (age range, 33–70 years). Other five patients with anaplastic glioma were excluded from this study.

2.2. Imaging protocol

CT examinations were performed on a 256-slice scanner (Brilliance iCT, Philips Medical Systems, Cleveland, OH, USA). This first scan served as a localizer to ensure that the whole tumor would be covered by the perfusion imaging field. Then, PCT imaging was performed in a continuous scanning pattern. PCT parameters were 80 kV and 100 mAs, 220 × 220 mm field of view [FOV], 512 × 512 matrix, and slice thickness of 5 mm. Perfusion scanning was performed after injection of 60 ml of non-ionic contrast agent containing 300 mg of iodine per ml (Omnipaque; GE Healthcare, Shanghai, China) at a rate of 5 ml/s. Eight seconds after starting the injection, 60 s continuous images at 1 s interval were acquired at the selected slice location, with a time period of about 70 s.

MR examinations were performed on a 3.0-T MR system (Verio, Siemens AG, Erlangen Germany) with a 16-element head matrix coil. The protocol for conventional MRI consisted of sagittal T1-weighted, axial T2-weighted, axial fluid attenuated inversion recovery, and axial T1-weighted sequences.

For DCE-MRI, two pre-contrast datasets were acquired using baseline T1-weighted MRI (repetition time [TR]/echo time [TE], 5.1/1.8 ms; [FOV], 240 mm × 240 mm; matrix, 138 × 192; slice thickness, 3. 6 mm) with flip angles of 2° and 15°; this was followed by DCE acquisition (TR/TE, 4.9/1.9 ms; FOV, 240 mm × 240 mm; matrix, 138 × 192; slice thickness, 3.6 mm) with a flip angle of 12°, consisting of 60 measurements with temporal spacing of 4.29 s. After the fifth baseline acquisition, a gadolinium (Gd)-based contrast agent, Gd-diethylenetriamine pentaacetic acid-bismethylamide (Gd-DTPA-BMA; Omniscan, GE Healthcare, Oslo, Norway) was injected via the antecubital vein as a bolus (rate, 4 ml/s; dose, 0.1 mmol/kg body weight), with a time period of about 280 s. Pre-and post-contrast T1-weighted imaging sequences were acquired in the same axial geometry.

2.3. Image processing and analysis

Image processing was carried out off-line. Raw PCT and DCE-MRI data were imported into the MIStar software package (Apollo Medical Imaging, Melbourne, Australia). Arterial input function was generated from a chosen section of the middle cerebral artery. PCT yielded permeability surface-area product (*PS*) using deconvolution physiological models, while DCE-MRI determined volume transfer constant (K^{trans}) using the Tofts-Kermode compartment model. Regions of interest (ROIs) were manually delineated on the tumors in *PS* and K^{trans} maps by an experienced neuroradiologist blinded to histological results. ROI size was kept constant (radius, 4–6 mm) for each tumor. Three ROIs were measured in each patient, and maximal *PS* and K^{trans} values were selected for analysis. Cystic, necrotic, and hemorrhagic regions, as well as normal microvessels within the ROIs, were avoided during ROI selection.

2.4. Immunohistochemistry (IHC) and microvascular density quantification

Immunohistochemistry was performed on 5 μm thick sections using a standard avidin-biotin-peroxidase technique with LSAB Kit (Dako Corporation, Santa Barbara, CA). Anti-CD105 primary antibodies (rabbit polyclonal, Dako) were used to quantify microvascular density (MVD). Each sample was microscopically assessed by an experienced neuropathologist. Microvessels showing brown signals were considered to be positive. Five separate areas (173 μm^2 each) in microvascular hotspots of each sample were captured using a charge-coupled device (CCD) camera, and analyzed with the Motic Images Advanced software (version 3.2, Motic China Group CO. Ltd.). Staining scores were derived by dividing positive areas by total areas. CD105-MVD was determined as the highest microvessel count in five high power fields (200-fold magnification) [8].