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Comparison of different population-averaged arterial-input-functions in dynamic contrast-enhanced MRI of the prostate: Effects on pharmacokinetic parameters and their diagnostic performance

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ABSTRACT

Purpose: To assess the effect of different population-averaged arterial-input-functions (pAIF) on pharmacokinetic parameters from dynamic contrast-enhanced MRI (DCE-MRI) and their diagnostic accuracy regarding the detection of potentially malignant prostate lesions.
Materials and methods: 66 male patients (age 65.4 ± 10.8y) with suspected prostate cancer underwent multiparametric MRI of the prostate including T2-w, DWI-w and DCE-MRI sequences at a 3 T MRI scanner. All detected lesions were categorized based on ACR PI-RADS version 2 and divided into 2 groups (A: PI-RADS ≤3, n = 32; B: PI-RADS >3, n = 34). In each DCE-MRI dataset, pharmacokinetic parameters (Ktrans, Kep and ve) and goodness of fit (chi^2) were generated using the Tofts model with 3 different pAIFs (fast, intermediate, slow) as provided by a commercially available postprocessing software. Pharmacokinetic parameters, their diagnostic accuracies and model fits were compared for the 3 pAIFs.
Results: Ktrans, Kep and ve differed significantly among the 3 pAIFs (all $p < .001$). Ktrans and Kep were significantly higher in group B compared to group A (all $p < .001$). For chi^2, lowest results (representing highest goodness of fit) were found for intermediate pAIF (chi^2 0.073). ROC analyses revealed comparable diagnostic accuracies for the different pAIFs, which were high for Ktrans and Kep and low for ve.
Conclusion: Choosing various pAIF types causes a high variability in pharmacokinetic parameter estimates. Therefore, it is of great importance to consider this as potential artifact and thus keep AIF type selection constant in DCE-MRI studies.

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1. Introduction

Over the last 2 decades, MRI gained a central role in the diagnosis of prostate cancer (PCa) [1]. Prostate MRI exams usually consist of T2-weighted sequences, diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI) [2]. Similar to tumors of other organ systems, PCa is characterized by a more pronounced contrast enhancement than normal prostate tissue, which is related to tumor angiogenesis [3]. The newly formed tumor vessels show an increased permeability compared to normal vessels. A high tumor vascularity is thought to be associated with poorer prognosis [4] and high microvessel density in tumorous lesions is predictive for disease progression [5]. Thus DCE-MRI is of high interest as a non-invasive method for assessment of tumor vascularity. Several studies reported the capability of DCE-MRI for PCa detection, localization, staging and monitoring [6–11]. In a recent European consensus meeting of leading clinicians and researchers in the field of PCa, DCE-MRI was recommended as part of the routine prostate MRI [2]. Subsequently, DCE-MRI was included in the "Prostate Imaging Reporting and Data System (PI-RADS)" by the European

Abbreviations: 95%-CI, 95% confidence intervals; AIF, arterial input function; ACR, American college of radiology; AUC, area under the curve; DWI, diffusion-weighted imaging; DCE-MRI, dynamic contrast-enhanced MRI; EES, extravascular/extracellular space; ESUR, European Society of Urogenital Radiology; iAIF, individual AIFs; Kep, efflux rate constant from EES to the plasma; Ktrans, influx volume transfer constant from plasma to EES; PAT, parallel acquisition technique; PCa, prostate cancer; pAIF, population averaged AIFs; ROC, Receiver operating characteristic curve; PI-RADS, Prostate Imaging Reporting and Data System; rm-ANOVA, Repeated-measures ANOVA; ve, EES volume fraction; VOI, volume of interest.

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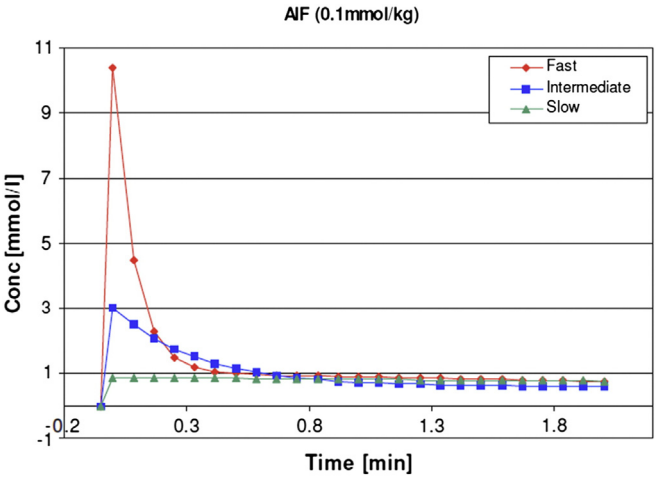

Fig. 1. Gadolinium concentration for "fast", "intermediate" and "slow" pAIF settings of MR Tissue4D (dose = 0.1 mmol/kg).

Society of Urogenital Radiology (ESUR) [12] and also in the recently revised PI-RADS v2, published by the American College of Radiology (ACR) [13].

DCE-MRI consists of multiple T1-weighted acquisitions before and after intravenous injection of a paramagnetic contrast agent, which causes changes of tissue T1 and T2 relaxation times depending on its accumulation in the tissue. After the contrast agent has been washed out of the tissue, tissue relaxation times return back to baseline. Assessment is either based on visual appraisal of the signal vs. time curve form, semi-quantitative or quantitative analysis of curve characteristics. Using quantitative assessment methods in DCE-MRI, it is possible to gain information about pharmacokinetic features related to vascular permeability, volume and perfusion of the extravascular/extracellular space (EES). For appropriate pharmacokinetic modeling, a vascular input function (arterial input function, AIF) is required [6,14]. For AIF extraction, different approaches have been proposed, such as individual AIFs (iAIF) [15,16] or population averaged AIFs (pAIF) [16–18]. In clinical practice, it is not always possible to estimate iAIF due to artifacts, e.g. in-flow or difficulties in the detection of supplying vessels, particularly in transversal slices, which are typically acquired for prostate MRI [19]. Therefore, pAIFs are often used, which are based on averaging iAIFs estimated from a representative group of patients [19]. Although pAIF does not take into account the individual patient hemodynamics, many studies have reported that pAIF provides individual and correct pharmacokinetic estimates, comparable to those derived when using iAIF [15–18]. Vendor-provided DCE-MRI analysis packages contain pAIFs from different populations with different signal intensity time courses (enhancement curves). The use of different AIFs is reported to be a source of variability among DCE-MRI studies, especially when multicenter studies are conducted. In this contribution, we aimed to assess the effect of different pAIFs on pharmacokinetic parameter estimates from DCE-MRI and their diagnostic accuracy regarding the detection of potentially malignant prostate lesions (i.e., PI-RADS >3).

2. Materials and methods

2.1. Patients

In this retrospective study, the institutional review board waived the requirement of informed patient consent. In the time between August 2014 and April 2015, 84 consecutive patients with elevated PSA levels and suspicious or inconclusive findings on transrectal ultrasonography were referred for multimodal prostate MRI. Of those 84 patients, 18 were excluded because of small lesion size (maximum diameter < 0.5 cm; 12 patients) and negative MRI findings (6 patients), resulting in a final sample size of 66 patients (age 65.4 ± 10.8 years). Two radiologists rated the likelihood of malignancy of detected lesions on multi-parametric MRI using the ACR PI-RADS v2, i.e. applying a 5-point rating scale (1: highly unlikely, 2: unlikely, 3: equivocal, 4: likely, 5: highly likely) [2,12,13]. Patients were then divided into 2 groups depending on PI-RADS score of the detected lesions (group A: PI-RADS ≤3; group B: PI-RADS >3).

2.2. Data acquisition

MRI examinations were acquired on a 48-channel 3 T scanner (MAGNETOM Skyra; Siemens Healthcare, Erlangen, Germany), using a 30-channel coil setup (18-channel body matrix coil + 12 channels from the spine array coil) for signal detection. Diagnostic prostate MRI consisted of T2-w TSE (refocusing angle, 136°; STH, 3 mm; TR, 4390 ms; TE, 90 ms; FOV, 199 × 199 mm^2), DWI-w (STH, 4 mm; TR,

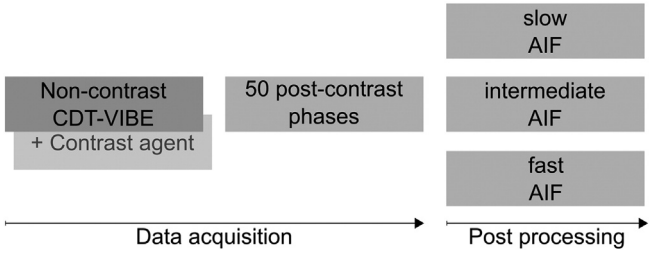

Fig. 2. Flowchart of data acquisition and parameter estimation.

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