Perfusion CT of the prostate: technical note and clinical applications

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Abstract

Objectives: The aim of this paper is to present in a simple concise and clear manner the computer tomography (CT) perfusion technique using a 64-multi-slice CT (MSCT) and to discuss the main clinical applications.

Materials and Methods: The CT protocol included: unenhanced CT scan to locate the prostate, intravenous administration of non-ionic iodinated contrast medium using a power injector (volume-100 ml, rate 5ml/s), scanning in CINE mode (cranio-caudal coverage - 40 mm, continuous exposure for 40 seconds) with a 10 seconds delay after beginning of injection, followed by ten additional 1-second scans in axial mode, with a 15-second interval to quantify the amount of contrast medium that filtered into the interstitial compartment. Perfusion CT examination was followed by a standard thoraco-abdomino-pelvic examination; a report was issued according to our daily clinical practice. The patients received doses (DLP - Dose Length Product) ranged between 1000 and 1500 mGy-cm, depending on their age and weight. Analysis of source images was performed on a workstation using a dedicated software.

Results: Colored functional maps and quantitative measurements were obtained for the following parameters: Permeability Surface-area product (PS), Blood Volume (BV), Mean Transit Time (MTT), Blood Flow (BF), Contrast Arrival Delay (IRF T0), Time to Peak (TTP), Transit Time to Impulse Residue Function Peak (Tmax). Placing ROI's in femoral artery, normal and abnormal prostate tissue, we obtained graphs with contrast-enhancement curves and tables with specific CT perfusion parameters.

Conclusions: Perfusion CT represent an imaging diagnostic tool that may be used in prostate cancer, allowing an easy and quick assessment of the functional changes, providing informations about in vivo tumor vascularity and guidance for histopathological correlation if biopsy is scheduled. Moreover, this technique may be performed in cases where MRI is contraindicated.

Key words: CT perfusion, functional CT imaging, prostate cancer
Clinical studies

Introduction and Objectives

Prostate cancer (PC) is the most common cancer in men, one of the leading causes of mortality due to the late diagnostic, in advanced stages of evolution [1]. Imaging techniques have an important role in cancer management including diagnosis, prognosis, planning therapy, and assessment of response to treatment. Using standard contrast-enhanced CT, even in cases with confirmed PC biopsy, prostate tumors are most often invisible and benign prostatic hyperplasia may mimic malignant enlargement. Difficulties in establishing an early and accurate diagnosis of PC led to research of new ways to explore the prostate such as functional imaging. One of them, with a potential for early detection of prostate cancer, is CT perfusion. Recent advances in CT technology permit to scan the entire prostate, the main advantage being accurately locating the tumor process [2]. The aim of this paper is to present in a concise, simple and teaching manner the prostate CT perfusion technique using a 64-Row Multidetector CT and to discuss the main clinical applications in prostate pathology.

Materials and Methods

CT perfusion technique

The prostate CT perfusion protocol was implemented on a MSCT equipment with 64-detector-rows (GE OptimaTM CT660). In the first phase, it is necessary to perform an unenhanced CT scan to locate the prostate. The patient is positioned in supine position and is advised to remain motionless throughout the examination, maintaining a superficial breathing. Before scanning, it is preferable to use a spasmolytic agent for reducing bowel peristalsis. The parameters for the unenhanced CT acquisition were as follows: helical mode; detector coverage – 40 mm; thickness – 5 mm; pitch – 1,375; rotation time – 0,7 sec.; smart mA (min. 100 – max. 440) with 40% dose reduction.

The cranio-caudal length of the volume coverage using the 64-detector-rows CT in CINE mode (continuous) is 40 mm, with the CT perfusion area positioned in a way that it can cover the entire prostate tissue as possible (Fig. 1). It is possible that in patients with important benign prostate hypertrophy the CT perfusion area is unable to cover the entire gland (the base and apex).

Intravenous administration of contrast material was performed using an automatic double-head injector (Nemoto Kyorindo Co., Ltd.). We have used 100 ml of non-ionic iodinated contrast medium (with a minimum concentration of 350 mg I/ml) which was administered intravenously through the right or left antecubital vein at 5 ml/s rate. Immediately afterward, was injected 50 ml of saline solution as a bolus (5 ml/s).

Scanning in CINE mode started with a delay of 10 seconds from the beginning of injection to enable acquisition of baseline unenhanced images and continued for a total of 40 seconds during the first pass. Eight contiguous 5-mm slices were obtained at 1-second intervals for each full rotation of the tube around the patient (3600), which means a total of 320 images (8x40). These scans were followed by ten additional 1-second scans in axial mode, with a 15-second interval to quantify the amount of contrast medium that filtered into the interstitial compartment (permeability surface-area product value, PS). The total time needed to acquire these images was 210 seconds, of which only 50 seconds was effective exposure to x-rays. The scanning parameters for CINE acquisition were: rotation time – 1 second; rotation length – full; detector coverage – 40 mm; collimation – 64 x 0,625 mm; space between the slices – 0; kV – 80; smart mA (min. 100 – max. 200); dose reduction – 40%; noise index – 11,57; DFOV – pelvis (35 x 35 cm); matrix – 512 x 512. For those ten additional scans we used the following parameters: axial mode, rotation time – 1 second, rotation length – full, detector coverage – 40 mm, axial thickness – 5 mm, number of images per rotation – 8i, kV – 80, smart mA (min. 100 – max. 200), dose reduction – 40%, noise index – 11,57; ISD – 15 seconds. Perfusion CT examination was followed by a thoraco-abdomino-pelvic examination that started with a delay of 220 seconds after the beginning of the intravenous contrast injection. The aim of this final scan was to identify distant spread of the tumor. A CT report was issued according to our daily clinical practice.

The dose received by patients (DLP - Dose Length Product) undergoing perfusion CT examinations varied
between 1000 and 1500 mGy·cm, depending on their weight and age, using an automatic exposure control in purpose to minimize radiation dose (ASIR - Adaptive Statistical Iterative Reconstruction).

**Image post processing**

Analysis of source images (Fig. 2) was performed on GE Advantage Workstation VolumeShare 5 with dedicated software – CT Perfusion 4D Multi-organs. An arterial input was defined placing a circular region of interest (ROI) within the best visualized artery (femoral) on the selected image, with fewer artifacts. Colored functional maps were generated using the software, included a color range from red to blue or purple. Quantitative measurements of different parameters for both tumor and glandular tissue were obtained and record-ed by manually defining regions of interest. A summary table of parameters and graph were obtained.

![Image of CT perfusion source images](image.png)

**Fig. 2** Examples of CT Perfusion -source images, from an 83-years old man with total PSA (prostate-specific antigen) of 54 ng/ml and histopathological diagnosis of acinar adenocarcinoma. Axial CT image (baseline) acquired at the beginning of the CINE acquisition before the arrival of contrast agent in arteries and into the prostate tissue (A) and after the contrast media arrived in the femoral arteries (arrow) and into the prostate (arrowheads) (B).

**Results**

Analysis of perfusion CT images. Colored functional maps and quantitative measurements were obtained for the following parameters:

- **Permeability Surface-area product (PS):** is related to the diffusion of some of the contrast agent through the pores of the capillary endothelium into the interstitial space; it is used to assess the permeability of blood vessels in tumor angiogenesis – is displayed in ml per 100 g of wet tissue per minute – ml/100 g/min (Fig. 3A) [3];
- **Blood Volume (BV):** is defined as the total volume of flowing blood in a given volume in the prostate – is displayed in ml per 100 g of prostate tissue – ml/100 g (Fig. 3B) [3];
- **Mean Transit Time (MTT):** is the average transit time of contrast agent in a given prostate region (indirectly reflect the local perfusion pressure) – is displayed in seconds (Fig. 3C) [3];
- **Blood Flow (BF):** is defined as the volume of blood moving through a given volume of prostate per unit time – is displayed in ml per 100 g of prostate tissue per minute – ml/100 g/min (Fig. 3D) [3];
- **Contrast Arrival Delay (IRF T0):** represents the time of arrival of the contrast agent to a given location (each tissue voxel) and is marked by the onset of tissue enhancement relative to the input artery – is displayed in seconds [3];
- **Time to Peak (TTP):** represents the time interval between the onset of the tissue enhancement and the peak of the tissue density curve – is displayed in seconds [3];
- **Transit Time to Impulse Residue Function Peak (Tmax):** represents the time passed until the contrast reaches a maximum in a given location compared with the input artery – is displayed in seconds and is the sum of MTT/2 and IRF T0 [3];
- **Mean Slope of Increase (MSI):** is computed as the average value of the slope function, which is estimated from the tissue density curve for each tissue voxel [3].

Placing ROI’s in femoral artery, normal and abnormal prostate tissue, we have obtained graphs with contrast-enhancement curves and with specific CT perfusion parameter values.

**Clinical applications.** The main clinical application of the prostate CT perfusion technique is to discriminate between malignant and benign lesions involving the prostate gland. In the following example, the patient with acute prostatitis (total PSA of 16,86 ng/ml) showed a peak of enhancement in the affected tissue at 188 sec-
seconds from the start of contrast injection (Fig. 4 - A, C, E). On the contrary, in a patient with proved prostate adenocarcinoma (total PSA > 100 ng/ml) the time passed until the contrast reaches the maximum peak was 34 seconds, with a descending curve (Fig. 4 - B, D, F). For comparative purposes, the table below shows the main parameters for those two patients: BV (ml/100g), BF (ml/100g/min), MTT (s) and PS (ml/100g/min) (Table 1).

<table>
<thead>
<tr>
<th>Type of prostatic lesion</th>
<th>PROSTATE - ACUTE INFLAMMATION (average)</th>
<th>PROSTATE CARCINOMA (average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BV</td>
<td>10.64</td>
<td>20.20</td>
</tr>
<tr>
<td>BF</td>
<td>33.82</td>
<td>104.00</td>
</tr>
<tr>
<td>MTT</td>
<td>21.45</td>
<td>11.92</td>
</tr>
<tr>
<td>PS</td>
<td>26.89</td>
<td>17.55</td>
</tr>
</tbody>
</table>

Comparing CT perfusion parameters, we can easily observe that there are large differences between CT perfusion vascular parameter values in PC and acute prostatitis: BV and BF values were higher in PC than acute prostatitis, but MTT and PS were lower. We believe that some values obtained in our examinations are different from literature data because of different CT equipment, protocol and software analysis used in other studies [4, 5, 6]. However, the data are consistent in terms of significant differences between the healthy and the affected prostate tissue.

**Discussion**

In the field of oncology, CT perfusion imaging has found applications for the detection, staging, prognostic assessment and observation of response to therapies. By providing an in vivo indicator of angiogenesis, the technique can be used for the diagnostic, risk stratification and therapeutic checking [7, 8].

The hypothesis that angiogenesis and lymphangiogenesis are important factors in the growth of malignant tumor [9], have led the researches to find new drugs targeting tumor vascularization [10, 11, 12]. For these reasons, microvessel density (MVD) is considered a gold standard method to measure aggressiveness of many cancers [13, 14]. Using the MVD were developed and improved new functional imaging techniques able to non-invasively quantify tumor microcirculation [15, 16]. In the last years, CT perfusion has been investigated to assess angiogenesis in malignant lesions of the brain, lung, liver, pancreas, esophagus, colon and rectum thanks to development of the functional techniques [4, 17]. Enhancement kinetics can be analyzed visually on the native images or on images after subtraction of the image acquired before contrast injection, focusing mainly on the speed of the filling phase (wash-in), peak intensity after this filling phase (peak), and the kinetics following this first phase - washout, plateau or slow accumulation (3).

The method was also used to realize qualitative evaluation of hemodynamic changes in prostate pathology [18]. In this direction, Osimani M et al. showed substantial differences in mean values of BV, MTT, and PS-area product parameters between PC, benign prostatic hypertrophy, chronic prostatitis, and healthy tissue and concluded that BV and PS-area product measurements obtained with perfusion CT have the highest correlation with immunohistochemical markers of angiogenesis in prostate cancer. Also, the technique may provide baseline perfusion values that could be well suited for monitoring tumor response to radiation or anti-angiogenic therapy [4].

Furthermore, the existence of a positive correlation between MVD and BV, MTT and PS, as well as relationship between high BF and high tumor grade may facilitate pretreatment indication of more aggressive carcinomas and hence, application of more aggressive treatment schedules / targeted therapies / anti-vascular therapy [5, 19].

Colored functional maps and quantitative CT perfusion parameters of the prostate gland provide relevant information about in vivo tumor vascularity. This goes...
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beyond the findings of previous studies that assessed the neovascularity of PC through microvessel density in histology. These maps allow easy and rapid visual assessment of the functional changes within the prostate gland, demonstrating the usability of this imaging modality in the clinical setting and, moreover, it provides guidance for histopathological correlation if biopsy is scheduled [6].

Cullu N et al. demonstrated that the performance of CT perfusion in PC detection was similar to that of MRI examination (T2-weighted image combined with diffusion weighted imaging), so the technique may be used in cases where MRI is contraindicated, such as pacemakers, claustrophobia and metallic implants [6].

However, Huellner et al. showed in their study a positive correlation between Gleason score and BF, and between PSA, BF and BV. A poor correlation was observed between Gleason score and BV. No correlation was found between MTT and PSA or Gleason score [20].

Our paper is focused especially on the presentation of the CT perfusion technique and vascular parameters used in prostate gland evaluation. Because of a small number of patients explored by CT perfusion we didn’t made a statistical analysis and we have not interpreted in depth the different vascular parameter values obtained using CT perfusion.

Conclusions

Perfusion CT represent an alternative imaging diagnostic tool that may be used in prostate cancer, allowing an easy and quick assessment of the functional changes, providing information about in vivo tumor vascularity and guidance for histopathological correlation if biopsy is scheduled. Moreover, the technique may be performed in cases where MRI is contraindicated.

Acknowledgment

This work received financial support through the project entitled „CERO – Career profile: Romanian Researcher”, grant number POSDRU/159/1.5/S/135760, co-financed by the European Social Fund for Sectorial Operational Programme Human Resources Development 2007-2013.

References