Optimization of perfusion CT protocol of renal cell carcinoma

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Aims and objectives

Perfusion computed tomography (CTp) is an imaging technique that provides qualitative and quantitative information regarding tumor angiogenesis [1,2]. It can quantify the real perfusion of tissues by applying mathematical models and dedicated software to calculate the delivery of contrast agent, and therefore blood, to tissues [3-4]. CT perfusion protocols depend on the scanning technique and mathematic modeling. Mathematic models are based on compartmental or deconvolution methods [1]. The analytical methods used (slope method, two-compartment, deconvolution, Patlak plotting) differ between vendor specifications [4-6]. In clinical studies published up to now both of these mathematic models are used for differentiation of histopathological types of renal tumors, including low- and high-grade clear cell renal cell carcinoma, for evaluation of response to anti-angiogenic treatment and ablative therapies [3, 7-9, 10-14].

The aim of the study was to determine methodological features of renal CT perfusion and to optimize the CTp of renal cell carcinoma (RCC).
Methods and materials

In our study 22 patients aged 44 to 76 years (mean age 61 years) with histologically proven clear cell renal cell carcinoma (ccRCC) were examined between February 2018 and October 2018. Male to female = 2:1. All of them were underwent renal CT perfusion imaging before surgical resection and pathological analysis in P. Hertsen Moscow Oncology Research Institute. Exclusion criteria were significant respiratory artifacts which couldn’t be reduced with post processing and previous antiangiogenic treatment.

All patients were examined with 80-sliced and 64-sliced scanners. Patients were required to breathe slightly to minimize respiratory artifacts. In addition a compression band was placed across the abdomen to reduce abdominal wall movement. An unenhanced CT scan of abdomen was performed to locate the renal mass. The supervising radiologist identified the tumor and placed the predefined scan volume of 4 cm to cover the lesion for the perfusion study. If the tumor was more than 4 cm and/or contained areas with necrosis the scan was selected in such a way to avoid the necrosis area as much as possible.

22 patients were divided into two groups depending on used scanning technique and mathematic modeling.

11 patients included to the first group were examined on 80-sliced CT scanner, perfusion was determined using compartmental model.

Compartmental analysis is based on single compartment or two-compartment model. The foundation of single-compartmental method is the Fick principle. It assumes that the intravascular and extravascular spaces are a single compartment and estimates tissue perfusion using the maximal slope or the peak height of the tissue concentration curve normalized to the arterial input function. A major disadvantage of this method is that the assumption of no venous outflow at the time of the maximum initial slope of the tissue timedensity curve is not always true.

Patlak plotting (two-compartment model) is a kinetic model that divides intravascular and extravascular components, the exchange between them is estimated (Fig 1). If this method of post-processing is used the following parameters are evaluated: blood flow (BF), blood volume (BV) and clearance.

The followed scanning parameters were used: scanning field of view 40 mm, 100 kV, 60-90 mA (depending on patient weight), 0.5 s gantry revolution time, 512x512 pixel, examination time 90 seconds. For perfusion imaging nonionic iodine contrast agent (volume 0.5 mL/kg of body weight, concentration 370 mg/mL) was injected in cubital vein at a flow rate 5.5-8 ml/sec followed by saline solution at the same volume and flow rate. The total duration of injection was 6-7 seconds.
11 patients included to the second group were examined on 64-sliced CT scanner, perfusion was determined using deconvolution method.

Deconvolution analysis is based on the use of arterial and tissue time-concentration curves to calculate the impulse residue function, which represents the fraction of contrast medium that remains in the tissue as time evolves after a bolus injection into the arterial input. Deconvolution-based method assumes that the concentration of contrast agent in the tissue is linearly depended on the arterial input and it is considered that BF is constant. In post-processing it is possible to estimate more than 10 quantitative characteristics, but usually only 4 mean parameters are measured: BV, BF, mean transit time (MTT) and permeability surface area product (PS). PS= clearance/unit volume.

The followed scanning parameters were used: scanning field of view 40 mm, 100 kV, 70-160mA (depending on patient weight), 2s gantry rotation time, 512x512 pixel, examination time 173 seconds. For perfusion imaging 60 ml of nonionic iodine contrast medium (concentration 350 mg/mL) was administrated intravenously at a flow rate 5ml/sec followed by 30 ml of saline solution at the similar flow rate.

Effective radiation dose was calculated in both groups.

Computed tomography perfusion parameters were measured by 2 independent radiologists (with 5 years of experience) who were blinded to the histopathological results.

In the first group the following parameters were measured and analyzed: BF, BV and clearance of tumor and normal renal cortex. At that BF was measured by using maximal slope method (it takes about 2-3 minutes) and BV and clearance were measured by Patlak plotting (it takes 10-15 minutes depending on examination).

In the second group BF, BV, MTT and PS of the tumor and normal renal cortex were measured and analyzed, it took about 5-8 minutes.
**Fig. 1:** Key stage of mathematical analyze using two-compartment model. A. Timedensity curve in tissue and artery (aorta) B. Patlak graph (the presence of selected section is necessary to create perfusion maps).

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Results

According to the study mean perfusion CT parameter values (BV, Clearance and BF or BF, BV, MTT and PS) for normal renal cortex and the renal tumors are summarized in Table 1 for the first group and in Table 2 for the second group.

Significant differences between RCC and normal renal cortex in all investigated parameters were found in both groups (P=0.001) Fig. 4-5.

Deconvolution is more simple method of postprocessing, it takes about 5 minutes. Patlak plotting is operator depending and very sensitive to image noise. The estimated effective radiation dose of the protocol used in the second group was controlled to within 22.9 mSv, which is above the effective radiation dose used for the first group (4.5+-1.2 mSv). To reduce the effective dose, we reduced the tubecurrent time product depending on the weight of patients.
**Fig. 2:** Perfusion CT parameter values in the first group.

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<table>
<thead>
<tr>
<th>Perfusion parameter</th>
<th>Normal renal cortex</th>
<th>RCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow</td>
<td>91,8 – 268,9 (std 52,7) ml/100g/min</td>
<td>55,7–194,8 (std 43,7) ml/100g/min</td>
</tr>
<tr>
<td>Clearance</td>
<td>30,43-69,74 (std 15,4) ml/100g/min</td>
<td>1,5-22,6 (std 11,4) ml/100g/min</td>
</tr>
<tr>
<td>Blood volume</td>
<td>26,2-45,3 (std 7) ml/100g</td>
<td>2,52-24,1 (std 12,3) ml/100g</td>
</tr>
</tbody>
</table>

**Fig. 4:** Perfusion maps of the patient with RCC from the first group measured by Patlak plotting. A- noncontrast CT scan, B-Equiv Blood volume (ml/100g), C-Blood flow (not the
final value, it should be calculated by slope-method), D-Clearance (ml/100g/sec). We see differences of all perfusion parameters between normal renal cortex and tumor.

Fig. 5: Perfusion maps of the patient with RCC from the second group measured by deconvolution method. A- Blood volume (ml/100g), B-Blood flow (ml/100g/min), C-Mean Transit Time D- Permeability (ml/100g/min). We see differences of all perfusion parameters between normal renal cortex and tumor.
<table>
<thead>
<tr>
<th>Perfusion parameter</th>
<th>Normal renal cortex</th>
<th>RCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow</td>
<td>242,8-301,7 (std 47,4) ml/100g/min</td>
<td>142,4-228,7 (std 51,2) ml/100g/min</td>
</tr>
<tr>
<td>Clearance</td>
<td>198,1-248,4 (std 31,7) ml/100g/min</td>
<td>88,9-103,4 (std 19,1) ml/100g/min</td>
</tr>
<tr>
<td>Equiv blood volume</td>
<td>90,8-102,4 (std 17,3) ml/100g</td>
<td>68,6-80,1 (std 18,7) ml/100g</td>
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**Fig. 3:** Perfusion CT parameter values in the second group.

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Conclusion

The Patlak and the deconvolution methods have its advantages and disadvantages.

The main advantage of the Patlak method is low effective radiation dose, but this method requires an experienced radiologist who can minimize noise and quickly perform post-processing.

The deconvolution method is easier to use, but the effective radiation dose is significantly greater than in the first case.

The following conditions may optimize the pCT of RCC: minimization of respiratory artifacts (slight breathing and abdominal belt) and reduction the effective dose by decreasing the tube current.

In perspective renal CT perfusion can be useful in differentiation of histopathological types of renal tumors, for evaluation of response to anti-angiogenic treatment and ablative therapies.
References