European Journal of Radiology Open 3 (2016) 95–99

Contents lists available at ScienceDirect

European Journal of Radiology Open

journal homepage: www.elsevier.com/locate/ejro

Comparison of organ-specific-radiation dose levels between 70 kVp perfusion CT and standard tri-phasic liver CT in patients with hepatocellular carcinoma using a Monte-Carlo-Simulation-based analysis platform

J. Gawlitza*, H. Haubenreisser, M. Meyer, C. Hagelstein, S. Sudarski, S.O. Schoenberg, T. Henzler

Institute of Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim, Medical Faculty Mannheim, Heidelberg University, Germany

ARTICLE INFO

Article history:
Received 24 April 2016
Accepted 25 April 2016
Available online 7 May 2016

Keywords:
Dynamic volume perfusion CT
Radiation dose
Organ specific
Dose
Hepatocellular carcinoma

ABSTRACT

Purpose: The aim of this study was to systematically compare organ-specific-radiation dose levels between a radiation dose optimized perfusion CT (dVPCT) protocol of the liver and a tri-phasic standard CT protocol of the liver using a Monte-Carlo-Simulation-based analysis platform.
Methods and materials: The complete CT data of 52 patients (41 males; mean age 65 ± 12) with suspected HCC that underwent dVPCT examinations on a 3rd generation dual-source CT (Somatom Force, Siemens) with a dose optimized tube voltage of 70 kVp or 80 kVp were exported to an analysis platform (Radimetrics, Bayer). The dVPCT studies were matched with a reference group of 50 patients (35 males; mean age 65 ± 14) that underwent standard tri-phasic CT (sCT) examinations of the liver with 130 kVp using the calculated water-equivalent-diameter of the patients. The analysis platform was used for the calculation of the organ-specific effective dose (ED) as well as global radiation-dose parameters (ICRP103).
Results: The organ-specific ED of the dVPCT protocol was statistically significantly lower when compared to the sCT in 14 of 21, and noninferior in a total of 18 of 21 examined items (all $p < 0.05$). The EDs of the dVPCT examinations were especially in the dose sensitive organs such as the red marrow (17.3 mSv vs 24.6 mSv, $p = < 0.0001$) and the liver (33.3 mSv vs 46.9 mSv, $p = 0.0003$) lower when compared to the sCT.
Conclusion: Our results suggest that dVPCT performed at 70 or 80 kVp compares favorably to sCT performed with 130 kVp with regard to effective organ dose levels, especially in dose sensitive organs, while providing additional functional information which is of paramount importance in patients undergoing novel targeted therapies.

1. Introduction

Tri-phasic contrast-enhanced abdominal computed tomography (CT) is the standard CT technique in patients with known or suspected hepatocellular carcinoma (HCC). However, optimal late arterial enhancement in patients with suspected HCC is often crucial leading to a suboptimal depiction of hypervascularized HCC lesions.

Dynamic volume perfusion-CT (dVPCT) is a rapidly developing technique, which allows the acquisition of morphological and functional perfusion information. In contrast to standard tri-phasic contrast-enhanced CT (sCT), dVPCT is based on the measurement of the temporal distribution of intra-venously injected contrast material by repeated scanning of the tissue of interest [1]. Functional dVPCT parameters provide several benefits within the context of oncological imaging. Faivre S et al. demonstrated that dVPCT parameters a more appropriate for response evaluation in patients with HCC undergoing sunitinib therapy when compared to RECIST [2]. In addition, several studies have demonstrated that dVPCT is a useful imaging biomarker in patients with HCC undergoing minimally invasive therapies like transarterial chemoembolization or transarterial radioembolization [3,4]. Besides advanced response evaluation, improved detection of hypervascular liver lesions [5]

* Corresponding author at: Institute of Clinical Radiology and Nuclear Medicine, University Medical Centre Mannheim (UMM), University of Heidelberg, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany.
E-mail addresses: Joshua.Gawlitza@medma.uni-heidelberg.de, joshua_gawlitza@yahoo.de (J. Gawlitza).

http://dx.doi.org/10.1016/j.ejro.2016.04.003

Table 1
Patient collectives.

	liver dVPCT protocol	triphaseal sCT
n	52	50
♂/♀	41/11	35/15
age ø	65	65
WED ø [mm]	307	307
CTDI ø [mGy]	23	11,89
DLP ø [mGy*cm]	1931	1936
70 kV/80 kV	39/13	

WED: Water equivalent diameter, DLP: Dosis length product.

as well as differentiation between hemangioma and hypovascular metastases has also been demonstrated for dVPCT [6,7].

However, despite the above mentioned benefits, dVPCT has not yet found its way into clinical routine. This is mainly due to concerns about high radiation dose levels and limited dynamic z-axis coverage with previous CT generation. Recently introduced state-of-the-art CT systems have enabled dVPCT studies performed with 70–80 kVp tube voltage covering whole anatomic regions or organs like the liver. The reduced tube voltage in dVPCT studies has the advantage to significantly reduce radiation dose levels while at the same time increasing contrast attenuation. However, low kVp dVPCT protocols potentially reduce radiation dose levels, there is still a lack of a detailed radiation dose evaluation of low kVp dVPCT protocols [8].

Thus, the aim of this study is to systematically evaluate organ specific radiation doses of a 70/80 kVp dVPCT liver protocol in patients with suspected HCC in comparison to a tri-phasic sCT protocol.

2. Materials and methods

2.1. Study design

This retrospective HIPAA compliant single-center study was approved by the institutional review board and complies with the Declaration of Helsinki. The analyzed datasets were acquired in the clinical routine and retrospectively matched. All dVPCT patients underwent the examination due to suspected or known HCC. To minimize body shape related radiation dose differences the comparison group that underwent a tri-phasic sCT protocol of the upper abdomen was retrospectively matched via the water equivalent diameter (WED) with the dVPCT protocol group (Table 1) [9]. Besides the organ specific dose analysis of the liver dVPCT and the comparison to the tri-phasic abdomen protocol, the dose values of the 70 and 80 kVp dVPCT protocols were compared to each other.

2.2. Patient characteristics

The liver dVPCT group consisted of 52 patients (41 males, mean age 65 ± 12.8 [range 33–92]) with suspected HCC. The reference sCT group that served for the radiation dose comparison consisted of 50 patients (35 males, mean age 65 ± 14 [range 20–87]) that underwent a tri-phasic sCT of the liver due to various indications.

2.3. CT protocols

2.3.1. Dynamic volume perfusion CT protocol

All patients underwent an examination on a 3rd generation dual-source CT system (Somatom FORCE, Siemens Healthcare Sector, Forchheim, Germany) using the following scan paramaters: 70 or 80 kVp tube voltage (80 kVp in patients with an body mass index >33), 189 mAs tube current time-product at 70 kVp; 220 mAs tube current time-product at 80 kVp, 48 × 1.2 collimation, 4-dimensional spiral mode with variable pitch with a z-axis coverage of 22.4 cm. In all patients 18 spiral acquisitions were performed with a variable interscan delay (2 × 3 s; 10 × 1.5 s; 3 × 6 s; 2 × 15 s; 1 × 18 s) resulting in a total acquisition time of 71.2 s. The first acquisition was started 10 s after the start of the contrast injection. For contrast injection, 50 mL of nonionic iodinated contrast medium (Iomeprol 400, Bracco Imaging S.p.A., Milan, Italy) were injected through an 18-gauge needle in a cubital vein at a rate of 5 cc/s using a power injector (Stellant® D CT Injection System MEDRAD, Inc., Warrendale, USA) followed by a 50 mL saline chaser injected at the same flow rate. All patients were instructed to hold their breath as long as possible in a mid-exhalation state. If breath hold was not possible anymore throughout the scan, patients were instructed to shallow breath only through their nose in order to minimize motion. The raw data of dVPCT were reconstructed using a medium sharp convolution kernel (Br 36) at a slice thickness of 1.5 mm and a 1.3 mm increment using filtered back projection (FBP). The mean DLP of the dVPCT was 1931 ± 565 mGy*cm.

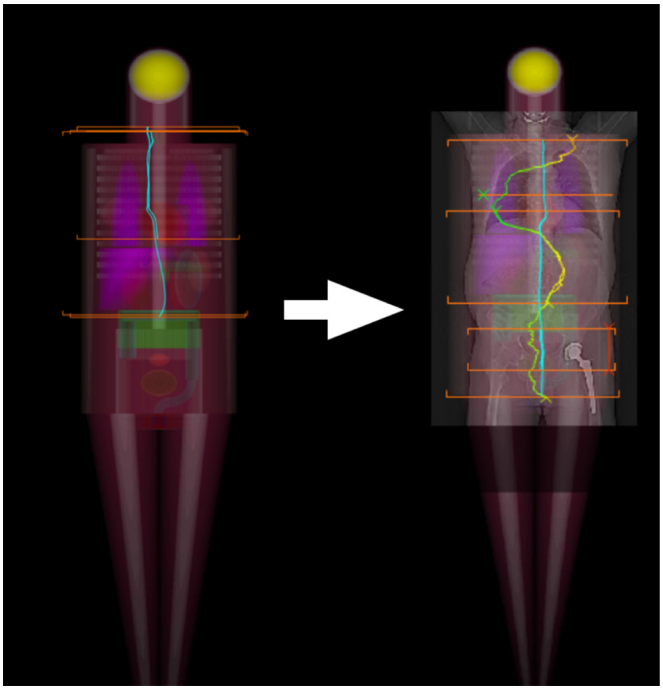

Fig. 1. automated matching of scanned CT images and digital pa5ent phantom.

2.3.2. Tri-phasic standard CT protocol

All patients of the reference sCT group underwent an tri-phasic CT of the upper abdomen on a clinical routine scanner (Somatom Emotion, Siemens Healthcare, Forchheim, Germany) using the following scanning parameters: 130 kVp tube voltage; 110 reference mAs tube current time product using automated tube current modulation (CareDose4D, Siemens Healthcare, Forchheim, Germany); 16 × 1.2 detector collimation, 0.8 pitch factor. All images were reconstructed using FBP with a slice thickness of 1.5 mm using a reconstruction increment of 1.3 mm and a soft tissue reconstruction kernel (B30s, Siemens Healthcare, Forchheim, Germany). After the non-contrast enhanced acquisition the arterial phase was performed with 80 cc of iodinated contrast material (Iomeprol 400, Bracco Imaging S.p.A., Milan, Italy) injected with 4 cc/s via an antecubital vein followed by a 50 mL saline chaser injected at the same flow rate. For the determination of the scan start the bolus tracking technique was used with a ROI placed within the abdominal aorta at the level directly below the diaphragm. After the trigger threshold of 100HU was reached the scan started after an additional scan delay of 10 s. The portal-venous CT acquisition was started 70 s after

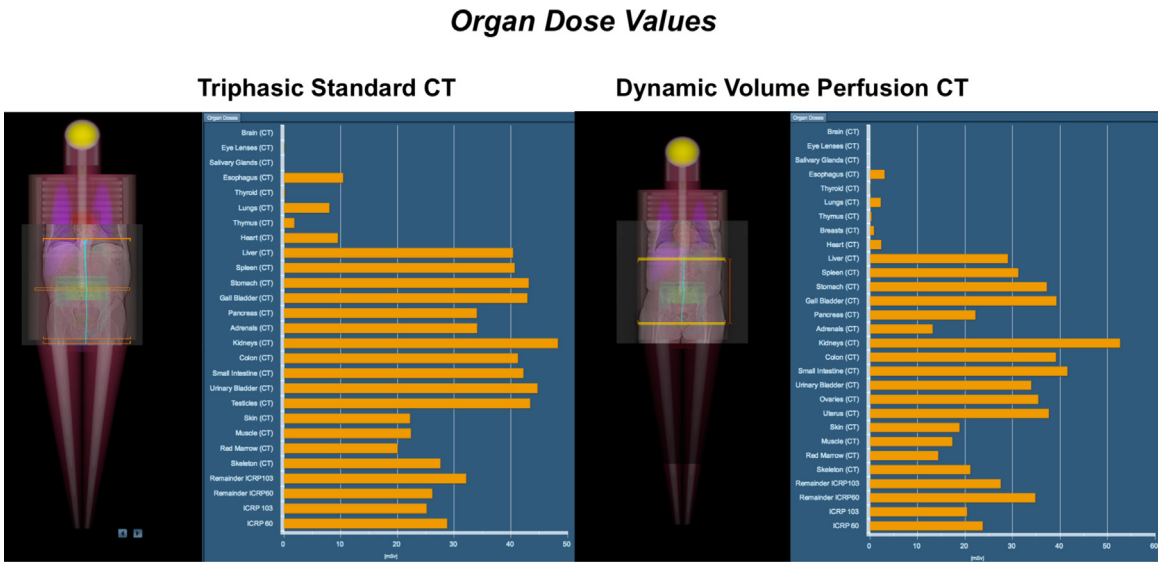

Fig. 2. Two exemplary, water-equivalent-diameter-matched exams of two males patients with suspected hepatocellular carcinoma. On the left side, the dynamic volume perfusion exam is shown, on the right side the triphasic standard CT.

the start of the contrast administration. The mean DLP of the sCT was 1936 ± 912 mGy*cm.

2.4. Radiation dose calculation

A Monte-Carlo-Simulation-based analysis platform (Radimetrics, Bayer Healthcare, Germany) was used to calculate the organ specific radiation dose values. Therefore the dVPCT and sCT datasets were uploaded to the capable, local analysis server. Afterwards the software automatically matches the phantom and the patient topogram (Fig. 1) and calculates the organ specific radiation dose (Fig. 2). Targets of the analysis were 17 individual organs (e.g. colon, gall bladder, red bone marrow etc.) as well as the global radiation parameter ICRP103.

2.5. Statistical analysis

The statistical analysis was performed using JMP 11 (SAS, Cary, USA). A two-tailed *t*-test (CI 95%, α 0.05) was performed to compare the organ specific doses of the dVPCT protocol with the ones of the sCT reference group as well as the doses of the 70 kV- with the 80 kV-liver dVPCT group. Additionally a non-inferior analysis was performed via an equivalent test, based on an one sided *t*-test. The non-inferior margin, the border which defines the new method (dVPCT) as non-inferior to the old (sCT), was set at 5% of the mean sCT dose of the individual examined organ/radiation parameter. A p-value of <0.05 was in all test considered statistically significant.

3. Results

3.1. Dynamic volume perfusion CT protocol

The mean DLP of the dVPCT protocol was 1931 mGy*cm (Table 1). The mean ICRP 103 was 22.6 mSv (±6.5 mSv; 10.9–34.5 mSv). With 49.7 mSv, 40 mSv and 38.4 mSv the kidneys, the gall bladder as well as the stomach were the organs with the highest radiation dose exposure. The lowest organ specific doses were calculated for the oesophagus (12 mSv) and the thymus (14.5 mSv). Radiation sensitive organs such as the colon and the red marrow were affected by 34.9 mSv respectively 17.3 mSv. Table 2 summarizes all radiation dose parameters for the investigated 17 organs in detail.

3.2. Comparison of radiation dose parameters between dynamic volume perfusion CT and standard tri-phasic CT

The comparison between the dVPCT and the standard tri-phasic CT has shown a significant dose reduction not only in the ICRP 103 but also in 12 out of 17 examined organs. Especially radiation sensitive organs like as the colon and the red bone marrow showed statistically significant lower organ dose values in the dVPCT cohort when compared to the sCT patient cohort (colon: 34.9 mSv dVPCT vs. 45.8 mSv sCT, p = 0.0011; red marrow: 17.3 mSv dVPCT: vs. 24.6 mSv sCT; p < 0.0001). The organ dose values of the heart, lungs, kidneys, skin and the thymus did not statistically differ between dVPCT and sCT acquisitions (p > 0.05). There was no statistically significant difference of the DLP between the matched tri-phasic sCT examinations and the dVPCT acquisitions (tri-phasic sCT: 1936 mGy*cm, SD = 912; dVPCT: 1931, SD = 565; p = 0.975) either. The global radiation parameter ICRP 103 was found to be statistically significantly lower in the dVPCT acquisitions when compared to the sCT acquisitions (dVPCT: 22.6 mSv, SD: 6.5; sCT: 31.7 mSv sCT, SD: 13,3; p < 0.0001). A detailed explanation of our results can be found in Table 2.

The non-inferiority analysis has shown a non-inferiority of the dVPCT in 16 out of 17 examined organs (Table 2).

3.3. Comparison between 70 and 80 kVp vs. dynamic volume perfusion CT radiation dose parameters

The comparison between the 70 kVp and 80 kVp dVPCT protocol revealed lower radiation dose values in 13 of the 17 investigated organs for the 70 kVp (Table 3) as well as in the ICRP 103. Beneath this lower affected organs were the muscles, the red marrow, the skeleton, the skin and the urinary bladder. Nevertheless only in 6 targets a significant difference between the 70 kVp and 80 kVp protocol has been proven: ICRP 103 (21.4 mSv vs. 26.37 mSv, p = 0.013), muscle (18.2 mSv vs. 26.1 mSv, p = < 0.0001), red marrow (16.1 mSv vs. 20.3 mSv, p = 0.0027), skeleton (28.76 mSv vs. 35.8 mSv, p = 0.0068), skin (21.59 mSv vs. 32.14 mSv, p = < 0.0001) and the urinary bladder (18.5 mSv vs. 38.7 mSv, p = 0.0154). In all examined targets, only the thymus has shown a lower organ specific dose in the 80 kV protocol (16.9 mSv vs. 8 mSv; Table 3).

Table 2
liver dVPCT protocol compared to the triphaseal sCT protocol.

	means [mSv]		standard deviation		equivalence test		two-tailed *t*-test	
	dVPCT	sCT	dVPCT	sCT	t-value	p-value	t-value	p-value
adrenals	23.9	40	22	14.3	4.92	<0.0001	4.42	<0.0001
colon	34.9	45.8	20	13.9	4	<0.0001	3.36	0.0011
esophagus	12	16.4	10.7	9	2.66	0.0046	2.25	0.0267
gall bladder	40.4	47.5	20	13.1	2.79	0.0031	2.1	0.0383
heart	18.3	24.2	20.2	17.6	1.89	0.0309	1.57	0.1192
ICRP103	22.6	31.7	6.6	13.3	5.12	<0.0001	4.3	<0.0001
kidneys	49.7	54.2	25.6	15	1.73	0.0431	1.09	0.2776
liver	33.3	46.9	20.9	15	4.4	<0.0001	3.79	0.0003
lungs	18.4	19.9	20.3	15.6	0.69	0.246	0.42	0.67
muscle	20.3	28	5.4	11.8	5.02	<0.0001	4.19	<0.0001
pancreas	23.9	39.4	17.2	12.6	5.82	<0.0001	5.2	<0.0001
red marrow	17.3	24.6	3.7	9.4	6.04	<0.0001	5.09	<0.0001
skeleton	30.5	38.5	9.4	19.1	3.34	0.0006	2.66	0.0097
skin	22.4	28	6.5	13.2	2.4	0.0092	1.69	0.095
spleen	31.5	46.8	21.9	14.6	4.78	<0.0001	4.17	<0.0001
stomach	38.4	49.4	21.1	14.6	3.73	0.0002	3.07	0.0028
thymus	14.5	7.8	23.6	12.6	−1.68	0.95	−1.8	0.0754
urinary bladder	25.1	48.6	20.2	17.7	6.88	<0.0001	6.25	<0.0001

dVPCT: Dynamic volume perfusion CT, sCT: Standard CT.

Table 3
Statistical analysis of the 70kV- and 80kV-liver dVPCT protocols.

	means [mSv]		standard deviation		two-tailed *t*-test	
	70 kV	80 kV	70 kV	80 kV	t-value	p-value
adrenals	22.86	27.85	22	24	0.63	0.5343
colon	30.85	43.1	17.8	23.8	1.6	0.12
esophagus	12.58	10.8	11.5	8.9	−0.5	0.58
gall bladder	38	47.9	17	26	1.23	0.23
heart	19.237	16.8	21.65	17	−0.4	0.69
ICRP103	21.4	26.37	6.5	5.2	2.69	0.013
kidneys	46.7	58.8	22.2	31.9	1.23	0.2381
liver	31.49	39	20	23.8	0.9	0.33
lungs	19.9	15.27	22	14	−0.8	0.41
muscle	18.2	26.1	3.75	4.78	5.25	<0.0001
pancreas	22.7	27.49	17	18.6	0.7	0.4407
red marrow	16.1	20.3	2.9	3.7	3.56	0.0027
skeleton	28.76	35.8	9.7	6.3	2.9	0.0068
skin	21.59	32.14	3.9	4.7	7	<0.0001
spleen	29.79	36.73	21	24.2	0.889	0.3862
stomach	36.3	45	19.6	24.5	1.1	0.2766
thymus	16.9	8	27	6.7	−1.8	0.0699
urinary bladder	18.5	38.7	13.8	23.9	2.775	0.0154

4. Discussion

Our study provides a systematically analysis of organ specific radiation dose values associated with dVPCT performed with 70 or 80 kVp. In addition, we compared organ dose values between dVPCT and a triphasic sCT protocol. Our results demonstrate, that dVPCT with low tube voltage settings lead to non-inferior radiation dose values when compared to sCT. Besides the fact, that the DLP of the dVPCT and the sCT did not statistically significantly differ our results show that in the majority of the examined organs the specific organ dose values were significantly lower in patients undergoing dVPCT at 70 or 80 kVp. Interestingly, the thymus was the only investigated organ in which the sCT protocol has lead to a lower organ specific radiation dose. The higher dose of the thymus could be explained by the shuttle-mode technique that was used for the dVPCT acquisitions. In this technique, the patients shuttles back and forth 18 times leading to a higher scatter radiation for organs outside of the scan field.

The radiation dose reduction for all other organs can be is explained by various factors. First, the main influence is most likely attributed the tube voltage reduction (70 or 80 kVp vs. 130 kVp). As shown in previous studies, a lower tube voltage leads to a significant reduction of the effective dose [8]. In the early development of perfusion CT a reduced tube voltage of 70–80 kV has already become the standard in order to minimize the total radiation dose during continuous scanning [10]. However, with the introduction of dVPCT over a larger z-axis the tube current of most clinically available CT systems was not sufficient in order to cover larger anatomic areas with low tube voltage settings [1]. The reduced tube current in combination with state of the art noise reduction algorithms and full digital CT detectors that reduce electronic noise are also responsible for the dose reduction of state-of-the-art dVPCT protocols [1]. It is of special importance, that iterative reconstruction techniques are currently not available for the reconstruction of dVPCT raw data. Therefore, one can expect that radiation dose reduction in dVPCT will further evolve once iterative reconstruction techniques will become available for dVPCT. The radiation dose values observed in our study are in accordance to previous studies that reported mean CTDIs of 12.4 mGy for 16-slice CTs (11.89 ± 4.47 in our study) and mean DLPs of 1831 mGy*cm for dVPCT (1931 ± 565 in our study) [11,12]. In contrast to those studies we did not only focus on global radiation parameters but also on organ specific radiation doses.

Our study has several limitations which have to be considered. First, we compared our dVPCT protocol with a sCT protocol on a 16 slice MDCT system equipped with automated tube current modulation but no iterative reconstruction and not automated tube voltage selection. Therefore, one has to acknowledge that our results are not necessarily representative for more recent CT systems with iterative reconstruction techniques as well as automated tube voltage selection and full digital detectors for dose reduction. However, 16-slice MDCT systems are still the most widely used systems world-wide. Moreover, even if state-of-the-art CT systems may lead to lower radiation dose levels when compared to our low tube voltage dVPCT our results indicate that dVPCT is not inevitably associated with higher radiation dose levels which is still the general perception of many radiologists. Within this context, one has to deliberate about whether patient benefit from additional functional information or whether the additional radiation dose has harmful effects for the patient. Second, our study population is relatively small and our results are not generally representative for all dVPCT acquisition techniques. Since, wider CT detectors are known to be less dose efficient our results should only be interpreted within the context of shuttle-mode dVPCT acquisitions.

In conclusion, our study demonstrated that dVPCT of the liver shows non-inferior radiation dose values when compared to a triphasic sCT acquisition. Thus, dVPCT could be used more widely in patients undergoing targeted therapies or minimally invasive therapies like transarterial chemoembolization or transarterial radioembolization.

Conflict of interest

All authors have read and approved submission of this manuscript. All authors have no conflict of interest to disclose.

References

[1] E. Klotz, U. Haberland, G. Glatting, S.O. Schoenberg, C. Fink, U. Attenberger, et al., Technical prerequisites and imaging protocols for CT perfusion imaging in oncology, Eur. J. Radiol. 84 (2015) 2359–2367.
[2] S. Faivre, M. Zappa, V. Vilgrain, E. Boucher, J.Y. Douillard, H.Y. Lim, et al., Changes in tumor density in patients with advanced hepatocellular carcinoma treated with sunitinib, Clin. Cancer Res. 17 (13) (2011) 4504–4512.
[3] V. Goh, Q.S. Ng, K. Miles, Computed tomography perfusion imaging for therapeutic assessment: has it come of age as a biomarker in oncology? Invest. Radiol. 47 (1) (2012) 2–4.
[4] C.S. Reiner, S. Gordic, G. Puippe, F. Morsbach, M. Wurnig, N. Schaefer, et al., Histogram analysis of CT perfusion of hepatocellular carcinoma for predicting response to transarterial radioembolization: value of tumor heterogeneity assessment, Cardiovasc. Intervent. Radiol. (2015).
[5] K. Hayano, G.S. Desai, A.R. Kambadakone, J.M. Fuentes, K.K. Tanabe, D.V. Sahani, Quantitative characterization of hepatocellular carcinoma and metastatic liver tumor by CT perfusion, Cancer Imaging 13 (4) (2013) 512–519.
[6] J. Singh, S. Sharma, N. Aggarwal, R.G. Sood, S. Sood, R. Sidhu, Role of perfusion CT differentiating hemangiomas from malignant hepatic lesions, J. Clin. Imaging Sci. 4 (2014) 10.
[7] M.A. Fischer, N. Kartalis, A. Grigoriadis, L. Loizou, P. Stal, B. Leidner, et al., Perfusion computed tomography for detection of hepatocellular carcinoma in patients with liver cirrhosis, Eur. Radiol. 25 (11) (2015) 3123–3132.
[8] M. Meyer, H. Haubenreisser, U.J. Schoepf, R. Vliegenthart, C. Leidecker, T. Allmendinger, et al., Closing in on the K edge: coronary CT angiography at 100, 80, and 70 kV-initial comparison of a second- versus a third-generation dual-source CT system, Radiology 273 (2) (2014) 373–382.
[9] M. Bostani, K. McMillan, P. Lu, H.J. Kim, C.H. Cagnon, J.J. DeMarco, et al., Attenuation-based size metric for estimating organ dose to patients undergoing tube current modulated CT exams, Med. Phys. 42 (2) (2015) 958–968.
[10] M. Wintermark, P. Maeder, F.R. Verdun, J.P. Thiran, J.F. Valley, P. Schnyder, et al., Using 80 kVp versus 120 kVp in perfusion CT measurement of regional cerebral blood flow, AJNR Am. J. Neuroradiol. 21 (10) (2000) 1881–1884.
[11] C. Frellesen, W. Stock, J.M. Kerl, T. Lehnert, J.L. Wichmann, C. Nau, et al., Topogram-based automated selection of the tube potential and current in thoraco-abdominal trauma CT—a comparison to fixed kV with mAs modulation alone, Eur. Radiol. 24 (7) (2014) 1725–1734.
[12] N. Bricout, L. Estrade, F. Boustia, E. Kalsoum, J.P. Pruvo, X. Leclerc, Reduced-dose CT protocol for the assessment of cerebral vasospasm, Neuroradiology 57 (12) (2015) 1211–1218.