Perfusion with 64-slice computed tomography (CT) of non-small cell lung cancer (NSCLC): a reproducibility study

Poster No.: C-1820
Congress: ECR 2011
Type: Scientific Paper
Authors: L. Calandriello, A. R. Larici, A. del Ciello, F. Maggi, T. Congedo, M. L. Vita, P. Granone, L. Bonomo; Rome/IT
Keywords: Lung, CT
DOI: 10.1594/ecr2011/C-1820

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

Lung cancer is the leading cause of cancer death in both men and women worldwide.

Tumors need added blood supply for growing and therefore angiogenesis is considered a key process in tumorigenesis. Anti-angiogenic therapies have yielded promising results in patients with non-small cell lung cancer (NSCLC) [1].

CT perfusion (CTP) can provide an in vivo marker of angiogenesis and can be used for monitoring therapeutic effect of anti-vascular treatment. Perfusion consists of rapid series of images acquired after intravenous iodinated contrast medium administration. First pass perfusion provides quantitative information of blood flow and blood volume, while delayed phase measures tumor permeability. According to the mechanism of action of a specific anti-angiogenic drug, different parameters should be used in the assessment of treatment response [2, 3].

In the last few years there has been a considerable improvement in the CTP technique, moving from single tumor level evaluation to whole tumor perfusion assessment, with most reliable results. Moreover, commercial automatic software have become available for perfusion parameter calculation.

Reproducibility and repeatability of techniques that have to be used over time, as in tumor's treatment response assessment, is mandatory. In literature, it has been performed one study of CTP reproducibility in patients with NSCLC, by using a 16-rows scanner [4]. In this study, Authors assessed tumor permeability on delayed images, without evaluating first pass perfusion, because of the low temporal resolution of the technique. To the best of our knowledge, no previous studies have been published on reproducibility of perfusion technique with 64-rows scanner.

So, the purpose of our study was to assess the reproducibility of first-pass CTP of NSCLC carried out with 64-rows CT.
Methods and Materials

Patient population

For this study we obtained institutional review board approval and patient informed consent, which included explicit approval of radiation exposure for research purposes.

From May 2009 to May 2010, 14 consecutive patients (9 male, 5 female; age range 52 - 85, mean age 72 years) with histologically proven operable NSCLC were prospectively enrolled.

Inclusion criteria were:

- patient older than 40 years;
- tumor size ranging between 2 and 8 cm (the maximum diameter that can be evaluated for a whole tumour perfusion assessment with techniques used);
- no pre-operative treatment (nor chemotherapy neither radiotherapy);
- no contraindications to iodinate contrast medium injection;
- patient capability of cooperating to the exam.

CT technique

All CT perfusion examinations were performed by using a 64-rows CT scanner (LightSpeed VCT, GE Medical Systems, Milwaukee, WI, USA). 50 ml of non ionic iodinated contrast medium (370 mgI/dl) were administrated at high injection rate (4-5 ml/s), followed by 20 ml of saline chaser at the same injection rate.

Two different CTP techniques were used according to the lesion’s maximum diameter. For lesions with maximum diameter up to 4 cm, a cine mode technique (continuous tube rotation with no patient table motion), consisting of 80 acquisitions encompassing the lesion site, was carried out with the following parameters: detector configuration 64×0.625 mm (total coverage 40 mm), reconstruction slice thickness 5 mm (8 images per rotation), tube voltage 80 kV, fixed tube current 200 mA, tube rotation time 0.5 sec, acquisition time 40 sec. Radiation dose delivered with cine mode technique was of 13.9 mSv.

For lesions with maximum diameter between 4 and 8 cm, a sequential mode technique, consisting of 17 successive acquisitions encompassing the tumor site, was carried out by means of two contiguous scans for each acquisition (shuttle technique). The following parameters were used: detector configuration 64×0.625 mm (coverage 40 mm), table movement 4 cm (total coverage 80 mm), reconstruction slice thickness 5 mm (8 images...
per rotation, 16 images for each pass), tube voltage 100 kV, fixed tube current 500 mA, tube rotation time 0.4 sec, acquisition time 46.6 sec. Shuttle technique delivered higher radiation dose than the cine mode technique (23.6 mSv).

Both dynamic CT techniques allowed to include the whole tumour during the first circulation of contrast medium (first pass assessment), with a start delay of 5 sec and a total duration scan time of 40-50 sec after bolus administration. All patients were trained to hold breath at end-inspiration during perfusion acquisition. Patients unable to keep holding their breath for the entire scan were asked to take very small breaths.

After 24 hours each patient underwent a second CTP acquisition by using the same technical parameters to assess reproducibility of both techniques. A total number of 28 CT dynamic scans, respectively 14 at time 0 (T0) and 14 at time 1 (T1), were obtained and analyzed for the entire study population.

**Image analysis**

CT perfusion data were transferred to a workstation (AW4.4, GE Medical Systems) and analyzed by using a commercial CT software (CT-Perfusion 4, GE Medical Systems, Milwaukee, WI, USA). First pass perfusion colored parametric maps were produced for each dynamic acquisition at T0 and T1.

Firstly, a circular ROI (region of interest) was placed in one artery included in the scan volume by using an electronic cursor and the mouse, to obtain the arterial input (arterial time-attenuation curve) (Fig.1). Usually it was selected aorta unless cases of apical lesions where aorta was not included in the volume and ROI was placed in carotid artery.

Secondly, a ROI was drawn freehand inside the lesion following the peripheral margin of the tumor to calculate perfusion parameters. Care was taken to exclude surrounding air and lung atelectasis.

The analysis was repeated for each contiguous transverse level, until the entire tumor had been covered (Fig.2). A global value of each perfusion parameter was calculated for the entire tumor by taking the mean value of all levels considered.

Perfusion parameters automatically calculated by the software included blood flow (BF), blood volume (BV), time to peak (TTP) and peak enhancement intensity (PEI) (Fig.3).

Bland-Altman statistic, expressed as standard deviation (SD) of the mean differences (#), was used to assess reproducibility of dynamic CT techniques among T0-T1 exams for each patient.
Results

Four out of fourteen patients were excluded from the study because of the poor quality of functional maps. In 2 cases, lesions were located near superior vena cava and perfusion assessment was hampered by beam hardening artifacts due to contrast medium administration (Fig.4). In the remaining 2 cases, motion artifacts caused perfusion CT failure.

Our final study population consisted of 10 patients. Six patients underwent sequential mode CT perfusion and four patients cinemode CT perfusion.

Eight out of ten tumors were located in the upper lobes and two in the lower lobes; seven were peripheral and three central.

Four lesions were adjacent to structures heavily affected by respiratory or cardiac movement, 2 near the heart border and 2 near the diaphragm.

Standard deviation of the mean differences (#±SD) between values of BV and BF obtained at T0 and T1 were respectively of -1.8±4.1 for BV and -0.6±3 for BF, thus demonstrating an overall good reproducibility. TTP and PEI assessment provide poor reproducibility (TTP: 3.4±23.3; PEI -9.8±17.1).

Good reproducibility was achieved for both cinemode and sequential mode techniques, as regards BV and BF (Tab.1).

Good results in terms of reproducibility for BV and BF were also observed for lesions placed in the upper lobes as well as in the lower lobes, as shown in Table 2.

Reproducibility was good for both central and peripheral lesions with slightly better results for centrally located (Fig.5) than the peripheral ones (Fig.6) (Tab.3).

An overall good reproducibility in terms of BV and BF was also obtained for lesions adjacent to structures affected by motion artifact (BV: -0.2±2.6; BF: -3.1±3.4) (Fig.7).
Conclusion

CT perfusion can be easily incorporated into the routine CT protocols.

One of the most important application of CTP in chest imaging is the evaluation of response to new anti-angiogenic agents in NSCLC. It has not yet been defined the best perfusion parameter for monitoring NSCLC treatment response. Nevertheless, there are evidence that when assessing tumor response, the mechanism of action of a specific anti-angiogenic drug may indicate which perfusion parameter has to be measured and hence the enhancement phase that has to be selected, first pass or delayed phases after 120 sec [3].

There is a number of studies in literature considering first pass phase parameters (blood flow and blood volume), as quantitative assessment of tumor perfusion, in the evaluation of anti-angiogenic treatment response [2,5]. According to Miles [3], the first pass phase typically comprises the first 45-60 sec immediately after intravenous injection and during this phase the contrast material is predominantly intravascular.

The first pass perfusion requires a high temporal resolution. In the era before 64-rows CT scanners, the high image frequency of first pass perfusion technique has restricted the volume of tissue that could be assessed [4].

A technique proposed in the assessment of treatment response over time must be reproducible and reliable. The only study in literature that tested CTP reproducibility in NSCLC was performed with a 16-rows CT scanner [4], by measuring tumor permeability with a delayed phase. In this study, first pass phase was not evaluated due to the low temporal resolution achievable with the scanner.

No previous studies have been published on the assessment of first pass perfusion reproducibility in patients with NSCLC, by using 64-rows CT scanner.

Our study tested two 64-rows CT dynamic techniques that allowed a whole tumor first pass perfusion analysis of lesions with maximum diameter up to 8 cm, demonstrating good results in terms of overall reproducibility for BV and BF. Good reproducibility regardless of tumor site was also demonstrated.

The main limitation of reproducibility of a technique that requires long lasting acquisition time when studying chest lesions, as perfusion technique, is the presence of respiratory or cardiac motion artifacts. Nevertheless, in our experience only two patients with motion artifacts were excluded from the evaluation and a good reproducibility in assessing lesions located near structures like heart and diaphragm was observed.

There are a few limitations to the present study. First, the sample size was small. But, also Ng et al. (2) included only 10 patients to test reproducibility of perfusion technique
with good results. Second, perfusion CT is associated with considerable irradiation to the patient and its use has to be well justified.

In conclusion, whole tumor first pass CTP has demonstrated good reproducibility in terms of blood volume and blood flow, also for lesions adjacent to structures affected by motion artifacts and thus it has the potential of being routinely used for monitoring treatment response in NSCLC. Nevertheless, further studies from larger patient population are needed.
References


3. Miles KA. Perfusion CT for the assessment of tumour vascularity: which protocol? BJR 2003;76:S36-S42

