Calculation of an individual dose of cytotoxic agents using CT volumetry of the lung for isolated lung perfusion and metastases resection

Poster No.: C-0271
Congress: ECR 2018
Type: Scientific Exhibit
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Keywords: Toxicity, Metastases, Cancer, Computer Applications-3D, Chemotherapy, CT, Thorax, Oncology, Lung

DOI: 10.1594/ecr2018/C-0271

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Aims and objectives

Pulmonary metastases occur in approximately 30% of patients dying of cancer. The 5-years overall survival of patients with pulmonary metastases after complete resection range between 20-40% [5]. One of the reasons for this rather poor survival rate is the high rate of local recurrence in the operated lung (from 43% to 66%) [4]. Poor results of systemic chemotherapy and surgical resection of pulmonary metastases are probably due the inability to achieve effective drug concentrations within the lung [1, 4]. Isolated lung perfusion (ILuP) is a surgical procedure during which the circulation of blood to the lungs is separated from the circulation of blood through the rest of the body, and a high doses of drug is delivered directly into the lung circulation to reduce the incidence of local pulmonary recurrence [3]. Procedures performed with melphalan or cisplatin at 37°C [3, 4, 6, 7]. The researchers use a standard dose of melphalan 45 mg [4]. The maximum tolerated dose of melphalan is 60 mg [3]. The researchers use a standard dose of cisplatin 70-200 mg/m² [6, 7]. However, this method of dosing cisplatin or melphalan does not take into account the individual characteristics of the lung. This may be the reason for insufficient dosage of cytostatic (lack of antitumor effect) or overdose of cytostatic (severe complications).

The aim of our study was to develop a technique for effective dosing of cytotoxic agents for ILuP with metastases resection using CT volumetry of the lung.
Methods and materials

This study consisted of the following steps:

1. Evaluation of the effectiveness of the software "Philips IntelliSpace Portal" for volumetry of the lungs. Fifty adult cancer patients whose lungs were unaffected by the disease underwent routine chest CT scans in 3-month intervals, resulting in a total number of 100 chest CT scans. Lung volume was calculated by semi-automatic software "Philips IntelliSpace Portal".

2. Evaluation of correlation between lungs volume and body surface area for fifty adult cancer patients. We calculated the volume of the right lung, left lung, two lungs and body surface area [2].

3. To develop a technique for effective dosing of cytotoxic agents for ILuP with metastases resection using CT volumetry of the lung. We selected 10 patients undergoing ILuP with cisplatin (120 mg/m$^2$) and metastases resection who had no severe complications after the procedure and there was no local pulmonary progression within 12 months. We selected 10 patients undergoing ILuP with melphalan (45-60 mg) and metastases resection who had no severe complications after the procedure and there was no local pulmonary progression within 12 months. Then we calculated the volume of these lungs and the dose of the cisplatin or melphalan was calculated per 1 ml of lung parenchyma.
Results

Results for each step:

1. Mean total lung volume was 5118 ± 1319 ml (Fig. 1) for the first routine chest CT scans and 5120 ± 1301 ml for the second chest CT scans. Mean left lung volume was 2419 ± 628 ml for the first chest CT scans and 2419 ± 636 ml for the second chest CT scans. Mean right lung volume was 2699 ± 702 ml for the first routine chest CT scans and 2700 ± 687 ml for the second chest CT scans. We found a strong positive correlation between the left lung volume at the first and second CT scans (Rs=0.94, p<0.001), right lung volume at the first and second CT scans (Rs=0.93, p<0.001), total lung volume at the first and second CT scans (Rs = 0.91, p <0.001) (Fig. 2). The mean difference between the volume of right and left lung was 10.4% (Fig. 3, 4)

2. Mean body surface area was 1.8 m$^2$ with the standard deviation of 0.2 m$^2$. We found a weak positive correlation between the left lung volume and body surface area (Rs=0.40, p<0.001), the right lung volume and body surface area (Rs=0.32, p<0.001), total lung volume and body surface area (Rs=0.32-0.40, p<0.001).

3. The average volume of the lung 10 patients undergoing ILuP with melphalan was 2592 ml. The average dose of melphalan per 1 ml of lung parenchyma was 50 mg / 2592 ml = 0.019 mg/ml. Thereby, for the individual calculation of the melphalan dose for the ILuP, we suggest using the method: $V_{\text{lung}} \times 0.019$ mg/ml. The average volume of the lung 10 patients undergoing ILuP with cisplatin (average dose 214 mg) was 2618 ml. The average dose of cisplatin per 1 ml of lung parenchyma was 214 mg / 2618 ml = 0.081 mg/ml. Thereby, for the individual calculation of the cisplatin dose for the ILuP with metastases resection, we suggest using the method: $V_{\text{lung}} \times 0.081$ mg/ml.
**Fig. 1:** Male, 35 years old. Total lung volume 6870.9 ± 88.6 ml

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**Fig. 2:** Correlation between total lung volume at the first chest CT scans and repeated chest CT scans (Rs=0.93, p<0.001)

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**Fig. 3:** Male, 35 years old. Right lung volume $3618.5 \pm 45.7$ ml

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**Fig. 4:** Male, 35 years old. Left lung volume 3252.3 ± 42.9 ml

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Conclusion

This method allows individual dosing of melphalan or cisplatin for isolated lung perfusion with metastases resection, taking into account the anatomical features of the lung and previous operations on the lung.
References


