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CASE REPORT

The application of 3D printing in the development of RECIST standard for evaluating tumor efficacy*

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Abstract

Three-dimensional (3D) printing technology, as a novel technical method, can convert conventional computed tomography (CT) or magnetic resonance imaging (MRI) scans to computer-aided design files and develop a 2D spatial structure into a 3D imaging structure. In recent years, the technology has been widely used in numerous areas, including head and neck surgery, orthopedics, and bio-medicinal research. This article uses examples of 3D printed tumor models to develop Response Evaluation Criteria In Solid Tumors (RECIST) standards to evaluate the changes in tumors. RECIST standard is currently recognized as the standard for assessment of chemotherapy. Under the RECIST standard, changes occurring in tumors before and after the surgery, are evaluated. The assessment depends upon a CT evaluation of the changes in the lesions with the largest diameters. In addition, the disease progression and stability of remission is also assessed. Three-dimensional printing technology is more intuitive in the evaluation of changes to human tumors following chemotherapy and targeted therapy. However, a few reports are available.

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Key words: Three-dimensional (3D) printing; RECIST standard; chemotherapy

Case 1: A 75-year-old man, diagnosed over half a month ago with a tumor in the left lung, was admitted to the hospital. In September 2015, obvious causes of cough, sputum, fever, and shortness of breath following activity, were not observed. In October 2015, the presence of a pulmonary hilar measuring 4.4 cm × 3.6 cm was detected in the left lung via a chest CT scan. (Fig. 1a). Multiple lymph node metastases were also noted. The pathological and immunohistochemical results were as follows: lower differentiation of adenocarcinoma, a wild-type EGFR gene, and an unfused EML4-ALK gene. Upon admission, no significant assessment result was noted, except for weak breathing sounds in the left lung. Based on clinical, pathologic, imaging, and preliminary assessment results, the patient was diagnosed with low differentiated adenocarcinoma of the left lung (IIIA, cT2N2M0). Pemetrexed, in combination with Endostar, was administered to the patient. The Chest CT results indicated that the left hilar mass was significantly reduced after two cycles of treatment. A part remission was indicated by the RECIST standard efficacy rating. Comparison of the two 3D print results were shown in Fig. 1b and 1c.

Case 2: A 66-year-old woman, experiencing chest tightness and heavy expectoration for 6 months, was admitted to the hospital. In February 2015, no apparent cause of chest tightness and cough white foam sputum was observed, and no system treatment was found. In August 2015, the aforementioned symptoms worsened. A CT scan revealed the presence of hilar lesions in the left lung (Fig. 2a). A physical examination indicated no abnormalities. Baseline examinations and CT scan results revealed presence of lesions measuring approximately 4.0 cm × 3.3 cm, in the left pulmonary hilum and left lung leaf with approximately 2.1 cm × 1.4 cm nodules. Central-type lung cancer with left lung lobe metastasis was considered.

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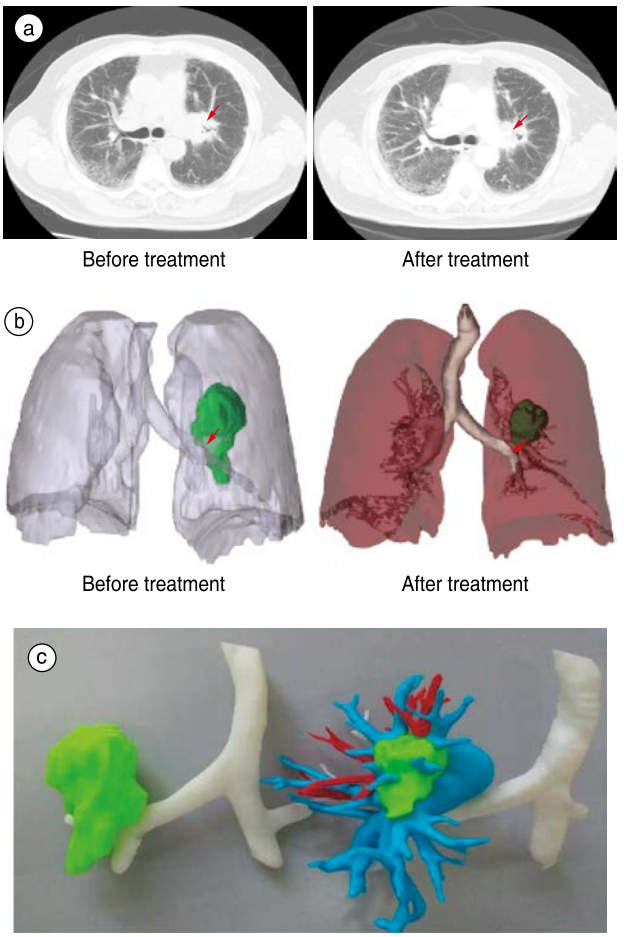

Fig. 1 (a) CT showed a change in the left lung mass before and after treatment; (b) 3D print before and after the treatment of left lung hilar mass change; (c) 3D print entity model diagram

The preliminary diagnosis was, presence of a lesion in the left lung space, and double lung metastasis. The patient and her family refused to undergo a bronchoscopy biopsy and chemotherapy and requested an oral targeted therapy. The patient was discharged. After 2 months, the patient was readmitted to the hospital. The CT scan results revealed the presence of lesions measuring approximately 5.0 cm × 3.3 cm in the left lung hilum and nodules measuring approximately 2.1 cm × 1.4 cm in the left lung leaf. Comparison of the two 3D print results were shown in Fig. 2b and 2c.

The cost and time of application of 3D printing technology

Approximately, one hour is required to design a 3D printing scheme on the computer. The printing of the 3D model requires approximately 3 to 5 h. The SD printing cost for each organ is approximately 3000 RMB.

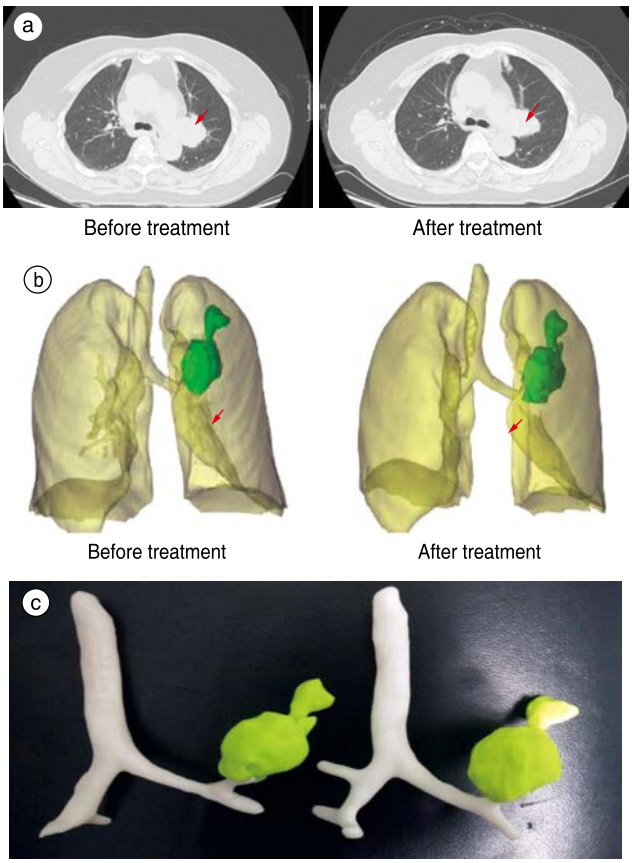

Fig. 2 (a) CT showed a change in the left lung mass before and after treatment; (b) Print before and after the treatment of left lung hilar mass change; (c) 3D print model diagram

Discussion

RECIST is a recognized assessment tool used to determine the changes in the tumors following chemotherapy and targeted therapy, and to evaluate the prognosis of patients. The assessment depends on CT imaging of target lesions with LD, and the sum of changes in patients with disease progression, and stable remission [1–2]. Provisions in the RECIST standard include a length of at least 2 slice thickness (10 mm) for a lesion (a thickness of less than 10 mm is considered to be normal in lymph nodes). onfusing. However, due to the conditional difference of CT imaging, the LD, measured in accordance with LD recist standards, may not be credible. The measurements may be influenced by various factors, such as the shape of target lesions, and thus cannot be a true assessment of the patient's prognosis [2–4]. Moreover, the LD cannot be used to measure tumor invasion. In some cases, the target lesion is not a small tissue necrosis, and as a result, changes in the tumor cannot be measured [5–7].

Three-dimensional printing technology employs hierarchical processing, and gradually superimposes layer

upon layer to generate a 3D entity. The technique uses 3D software and tools to compile information from CT and MRI scans into a CAD file. The 2D cross section is then used to develop a 3D image [8]. The 3D printing technology, makes up for the lack of sensitivity of the RECIST standard in the evaluation of disease progression, remission, and stability [9]. Three-dimensional printing technology has been used in the field of medicine, as it captures the arbitrary complex geometry of the entity [9–11]. This technology allows the surgeon to understand the anatomy of the lesion [12]. The establishment of models of the head and neck, heart, pelvis, lung blood vessels, other related tissues and organs, as well as the in vitro simulation of the operating processes may improve the probability of a successful surgery [10–11, 13–15]. In medical oncology, 3D printing technology aids in the visualization of tumor volume and determination of tumor location and surrounding blood vessels. Moreover, it may enable the comprehension of blood flow distribution in the tumor and may provide a better observation index for the treatment [9, 14]. According to literature [16], 3D printing can also be used as a tool to study metastatic lesions and assess drug sensitivity. The 3D printing technology allows a simulation of malignant tumors within the human body and facilitates an intuitive understanding of tumor volume changes directly with a specific anatomical model interaction. As a result, patients are better able to comprehend the changes in the tumor volume. This understanding limits the dependence on imaging science, and allows direct communication between patients and healthcare providers [9]. Moreover, 3D printing technology also requires less materials and reduces labor and production costs [8].

In this paper, the CT results of two cases of lung tumor were compared with 3D printed models. The results indicate a more intuitive and comprehensive understanding of the effect of chemotherapy and targeted therapy on the changes to the tumor volumes, before and after the treatment. Among the two cases of clinical studies using 3D printed models of lung tumors, significant reduction in the volume of lung tumor of one patient was observed. However, in the second patient no significant change in the lung tumor volume was observed. However, the results indicated that a 3D printed model can provide better understanding of the volume changes in the tumor before and after the treatment. Three-dimensional printing is also more convenient and facilitates better communication between doctors and patients. With constant breakthroughs in technology and large-sample clinical research, 3D printing technology is expected to influence future treatments, probably in precision medicine. It can also enable the development of a customized treatment plan, tailored for the patient's specific conditions. The technology may also be extended to other applications and become a routine procedure in the future. Three-dimensional printing, as a novel technology, has not been widely promoted. Its application requires additional clinical randomized control trials, large-sample control studies, and long-term prognosis and follow-up support.

Conflicts of interest

The authors indicated no potential conflicts of interest.

References

1. Hu J, Tan BX, Liu M, *et al*. Late course three-dimensional conformal radiotherapy for esophageal carcinoma. Chinese-German J Clin Oncol, 2011, 10: 147–149.
2. Therasse P, Arbuck SG, Eisenhauer EA, *et al*. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst, 2000, 92: 205–216.
3. Nishino M, Cardarella S, Jackman DM, *et al*. RECIST 1.1 in NSCLC patients with EGFR mutations treated with EGFR tyrosine kinase inhibitors: comparison with RECIST 1.0. AJR Am J Roentgenol, 2013, 201: W64–W71.
4. Beaumont H, Souchet S, Labatte JM, *et al*. Changes of lung tumour volume on CT - prediction of the reliability of assessments. Cancer Imag, 2015, 15: 17.
5. Sakao Y, Kuroda H, Mun M, *et al*. Prognostic significance of tumor size of small lung adenocarcinomas evaluated with mediastinal window settings on computed tomography. PLoS One, 2014, 9: e110305.
6. Sakao Y, Nakazono T, Tomimitsu S, *et al*. Lung adenocarcinoma can be subtyped according to tumor dimension by computed tomography mediastinal-window setting. Additional size criteria for clinical T1 adenocarcinoma. Eur J Cardiothorac Surg, 2004, 26: 1211–1215.
7. Sakao Y, Miyamoto H, Sakuraba M, *et al*. Prognostic significance of a histologic subtype in small adenocarcinoma of the lung: the impact of nonbronchioloalveolar carcinoma components. Ann Thorac Surg, 2007, 83: 209–214.
8. Eisenhauer EA, Therasse P, Bogaerts J, *et al*. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer, 2009, 45: 228–247.
9. AlAli AB, Griffin MF, Butler PE. Three-dimensional printing surgical applications. Eplasty, 2015, 15: e37.
10. Sodian R, Weber S, Markert M, *et al*. Pediatric cardiac transplantation: three-dimensional printing of anatomic models for surgical planning of heart transplantation in patients with univentricular heart. J Thorac Cardiovasc Surg, 2008, 136: 1098–1099.
11. Witschey WR, Pouch AM, McGarvey JR, *et al*. Three-dimensional ultrasound-derived physical mitral valve modeling. Ann Thorac Surg, 2014, 98: 691–694.
12. Schmauss D, Gerber N, Sodian R. Three-dimensional printing of models for surgical planning in patients with primary cardiac tumors. J Thorac Cardiovasc Surg, 2013, 145: 1407–1408.
13. Chae MP, Rozen WM, McMenamin PG, *et al*. Emerging applications of bedside 3D printing in plastic surgery. Front Surg, 2015, 2: 25.
14. Nakada T, Akiba T, Inagaki T, *et al*. Thoracoscopic anatomical subsegmentectomy of the right S2b + S3 using a 3D printing model with rapid prototyping. Interact Cardiovasc Thorac Surg, 2014, 19: 696–698.

15. Akiba T, Nakada T, Inagaki T. Simulation of the fissureless technique for thoracoscopic segmentectomy using rapid prototyping. Ann Thorac Cardiovasc Surg, 2015, 21: 84–86.
16. Zhu W, Holmes B, Glazer RI, *et al*. 3D printed nanocomposite matrix for the study of breast cancer bone metastasis. Nanomedicine, 2016, 12: 69–79.

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