Transbronchial lung cryobiopsy guided by virtual bronchoscopy navigation in a child with diffuse alveolar hemorrhage syndrome:a case report

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Abstract

there are several advantages to the use of transbronchial lung cryobiopsy (TBLC), including less trauma, fewer complications, large and high-quality specimens, and lower cost. This procedure is mainly used for the etiological diagnosis of diffuse parenchymal lung diseases (DPLD) [2] and its most common complications, including bleeding and pneumothorax. Virtual bronchoscopy navigation (VBN) can assist bronchoscopists in pinpointing the target area in the lung and designing an appropriate navigation pathway to accurately reach the target lesion [3]. Thus, VBN improves the rate of diagnosis and reduces the risk of bleeding and pneumothorax. In this report, which we believe to be the first of its kind, we performed TBLC guided by VBN.

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To the Editor,

Diffuse alveolar hemorrhage syndrome (DAHS) is a life-threatening clinical syndrome caused by a variety of etiological factors. The main manifestations are hemoptysis, anemia, hypoxic dyspnea, and respiratory failure, while diffuse infiltration shadows are observed on both lungs on imaging [1]. DAHS can occur at

different ages in children, and there is great heterogeneity in its clinical manifestation and etiology. Treatment options vary for different etiologies. The complex etiology of DAHS means that any damage to the pulmonary microcirculation may lead to alveolar hemorrhage. Thus, early identification and etiological diagnosis, in particular, are both challenging and critically important. Compared with procedures such as surgical lung biopsy (SLB), there are several advantages to the use of transbronchial lung cryobiopsy (TBLC), including less trauma, fewer complications, large and high-quality specimens, and lower cost. This procedure is mainly used for the etiological diagnosis of diffuse parenchymal lung diseases (DPLD) [2] and its most common complications, including bleeding and pneumothorax. Virtual bronchoscopy navigation (VBN) can assist bronchoscopists in pinpointing the target area in the lung and designing an appropriate navigation pathway to accurately reach the target lesion [3]. Thus, VBN improves the rate of diagnosis and reduces the risk of bleeding and pneumothorax. In this report, which we believe to be the first of its kind, we performed TBLC guided by VBN.

An 8-year-old girl was admitted to the hospital after suffering from intermittent hemoptysis for more than 1 year, accompanied by anemia. Enhanced computed tomography (CT) scan of the chest and macrovascular reconstruction suggested that the transparency of the lung field was decreased. Diffuse pale shadows were seen in both lungs, which showed intensification after enhancement, and some of the pulmonary vessels had thick peripheral diameters (Figure1 A). A bronchoalveolar lavage fluid smear showed increased numbers of hemosiderin-laden cells, while special staining showed the presence of iron. Thus, an initial diagnosis of DAHS was made. To further identify the pathogenic basis, we attempted to obtain frozen lung tissue specimens by TBLC. To reduce the risk of bleeding and pneumothorax and make the biopsy procedure safer, we combined TBLC with VBN. Before the surgery, the respiratory physicians, radiologists, anesthesiologists, and pathologists were brought together to conduct a multidisciplinary discussion and jointly formulate a surgical plan and risk prevention and control plan. The parents of the child signed the informed consent for the surgery.

Endoscopic technique

Before the operation, high-resolution CT data (slice thickness 1 mm, spacing 0.6 mm) was imported into the navigation system (Archimedes VBN, Broncus Medical, USA) for the automatic reconstruction of 3D bronchial and vascular models. Sub-branches of the right lower lateral basal segment and posterior basal segment (which have fewer peripheral vessels, lower risk of bleeding, and avoid larger blood vessels) were chosen as the target positions. After determining the relationship between the biopsy target site and the peripheral vessels (as well as distance from the pleura), automatic calculation of the route and distance of the bronchoscope to the biopsy site was carried out. The operation was performed using rigid bronchoscopy sheath ventilation (STORZ, USA, No.4.5, outer diameter 7.3 mm, inner diameter 6.6 mm) under general intravenous anesthesia. A flexible bronchoscope was inserted through a rigid bronchoscopy sheath. Routine bronchoscopy (outer diameter 4.0 mm, orifice 2.0 mm; Olympus, Japan) was performed to exclude mucosal lesions, and bronchoalveolar lavage was performed in the middle lobe of the right lung. Then, under the guidance of the flexible bronchoscope, an occlusion balloon (6×30 mm, , Boston Scientific, USA) was placed in front of the opening of the right lower lobe (Figure 2 B), and gas was injected to inflate the balloon via the flexible bronchoscope. When the injected volume was sufficient to cause complete occlusion of the opening of the target bronchial lobe, the required gas volume was recorded, and the air tightness of the balloon was tested. The balloon was then deflated for standby use. The navigation guide line and airway data were displayed synchronously in real time via the endoscopic image. After the flexible bronchoscope reached the target lesion area, the lumen secretions were aspirated. When the puncture site was reconfirmed, the pressure of the carbon dioxide cryopexor (1.0 mm cryoprobe, Erbe, Germany) was set at 55–65 bars, a 1.0 mm cryoprobe was connected, and the freezing time was set to 10 s (based on the freezing effect of the cryoprobe in a water bath before the operation); a specially assigned person was responsible for the countdown reminder. After the guide sheath was inserted via the working channel of the flexible bronchoscope, the cryoprobe was inserted into the sheath and then placed in the target position under the guidance of the flexible bronchoscope. The distance from the front end of the cryoprobe to the pleura was confirmed by C-arm X-ray (Figure 2C, D). As the foot pedal of the cryopexor was depressed, a 10-s countdown was started. When the countdown

prompt tone sounded, the cryoprobe and the flexible bronchoscope were withdrawn, and, at the same time, the assistant quickly injected gas into the preset balloon for occlusion. The frozen tissue was placed on a glass slide for size measurement after the cryoprobe was thawed, and neutral formalin fixative was added for preservation. The flexible bronchoscope was then reinserted into the target lumen; after observation for approximately 1 min, it was confirmed that there was no blood leakage, and the balloon was released slowly and replaced next to the lobe segment to be occluded. Specimens were collected four times with repeated freezing. Specimen diameter was between 4 mm and 6 mm (Figures 2 F). When no active bleeding was observed, the bronchoscope was withdrawn and anesthesia recovery was started. The child had stable vital signs after the operation, and no complications such as hemoptysis or pneumothorax occurred. One week after the operation, the pathological results were reported. Light microscopy of the bronchoalveolar lavage fluid revealed a large number of degenerated red blood cells in the smear, as well as many hemosiderin-laden cells; special staining showed the presence of iron. The lung tissue biopsies permitted analysis of alveolar and bronchial structures. Hemosiderin-laden cells were observed in the alveolar cavity, and the alveolar septa showed widening as a result of lymphohistiocytic infiltration. In addition, lymphocyte foci were aggregated around the airway, and part of the vascular wall structure was destroyed and thickened. Furthermore, there was crystalline deposition around the vascular wall, and multinucleated giant cells were observed (Figure G). Following a diagnosis of pulmonary vasculitis, regular glucocorticoid therapy was performed, and regular outpatient follow-ups were performed. The patient did not experience hemoptysis again, and, after 3 months of treatment, lung imaging revealed obvious improvement (Figure 2H).

A large number of studies have shown that the etiological diagnosis rate achieved by TBLC in DPLD is more than 80%, with a low incidence of serious complications[7-8]. Thus, as a minimally invasive method for the diagnosis of DPLD, TBLC is considered a promising alternative to SLB [9-10]. However, there is limited knowledge of the suitability of TBLC for use in children, as the characteristics of airway development in children differ from those in adults. In one study, Moslehi et al. [11] performed TBLC in younger children (17 out of 28 were younger than 4 years old) and achieved a diagnostic rate of 92.8%. Nonetheless, TBLC can cause complications such as bleeding and pneumothorax. Based on conventional virtual navigation, the Archimedes system combines augmented reality and vessel mapping technology and can integrate spatial information relating to the airway and adjacent blood vessels, as well as distance from the pleura. Virtual bronchial trees can be reconstructed based on thin-slice CT, with the target lung lesions being indicated, and the biopsy pathway and procedure plan can be formulated to accurately avoid blood vessels; distance from the pleura and biopsy depth can also be measured. This technique has significantly improved the accuracy of bronchoscopy for in-depth diagnosis of the terminal lung regions and provided safer guidance for lung biopsies[5]. However, its application as a biopsy method in children with diffuse lung disease has not yet been reported.

In this article, our results show that using VBN is a feasible way to assist TBLC in order to conduct safe and accurate biopsy operations in children with DPLD. The experience gained from this case is summarized as follows. To perform the operation safely, we recommend that that TBLC should be performed by skilled surgeons, with the children under general anesthesia to avoid poor cooperation. For diffuse lesions, larger blood vessels should be avoided for biopsy; in this case, two sub-segments were chosen for lung biopsy to improve the diagnostic rate. For diffuse pulmonary lesions, the basal sub-branch of both lungs is preferred, especially the lumen of the lateral and posterior bronchial sub-segment, as this is relatively straight and unobstructed. Thus, it is easy to reach and is unlikely to become adhered to the adjacent vascular wall during the withdrawal of the cryoprobe, which would affect the sampling process. The freezing effect was tested repeatedly according to the diameter of the cryoprobe and the pressure of the gas source in this study. In terms of freezing effect and safety, the freezing time of the 1.0 mm cryoprobe was set to 10 s each time, and no intraoperative or postoperative bleeding or pneumothorax occurred. In addition, it is worth noting that attention should be paid to intraoperative changes in tidal volume (i.e., lung volume) in children. As the airway is occupied during bronchoscopy, air leakage may occur during mechanical ventilation. This means there may be a great difference between the actual tidal volume and the tidal volume set by mechanical ventilation. Such differences may bring about a change in lung volume, which will directly affect

navigation accuracy and operation safety. Thus, it is necessary to adjust the biopsy site according to ventilator parameters during the operation and review the target site again using the C-arm.

Following this initial application of VBN-guided lung biopsy and TBLC technology in children, it will be necessary to conduct further clinical explorations with larger sample sizes in the future. We believe that, with the safety advantage that comes from combining VBN and TBLC, the application of this technique will become widespread in children, further promoting the transformation from conventional empirical diagnosis to a more accurate and minimally invasive diagnosis mode. Through the combination of clinical imaging in pathology and upgrading of the technology, it is expected that the diagnosis of DPLD in children will reach a new level.

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Authors' contributions

All the Authors have revised the manuscript and contributed to the drafting of the article. They confirm that the manuscript is an original version and has not been published in any other scientific Journal or elsewhere. HM and FW have conceived the report; HM and MM have contributed to the patients evaluations and written the related comments; HM、ET and FW have designed and drafted most of the report. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the

corresponding author upon reasonable request.

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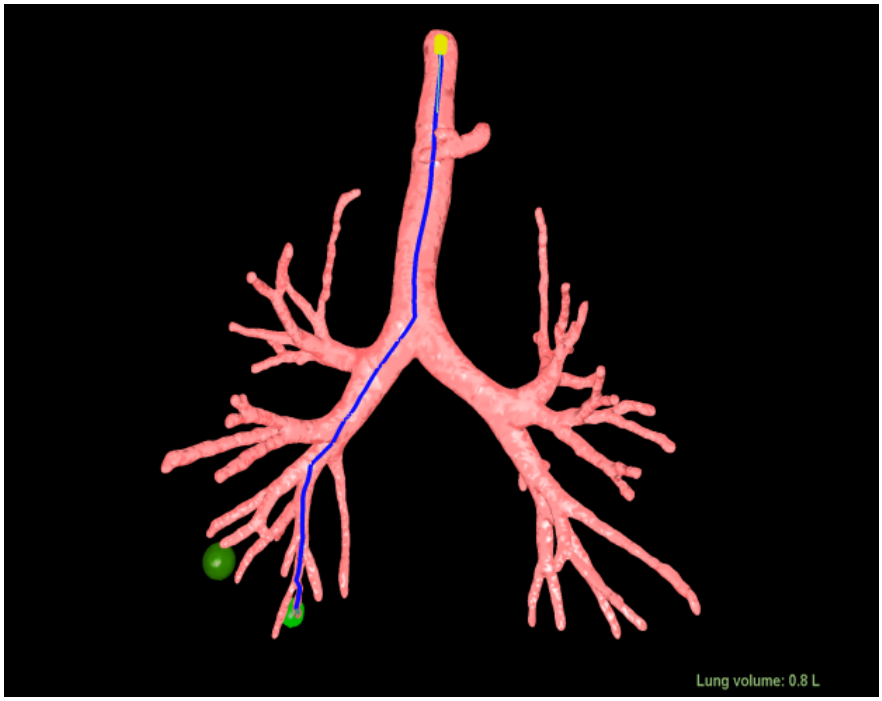
Figure 1



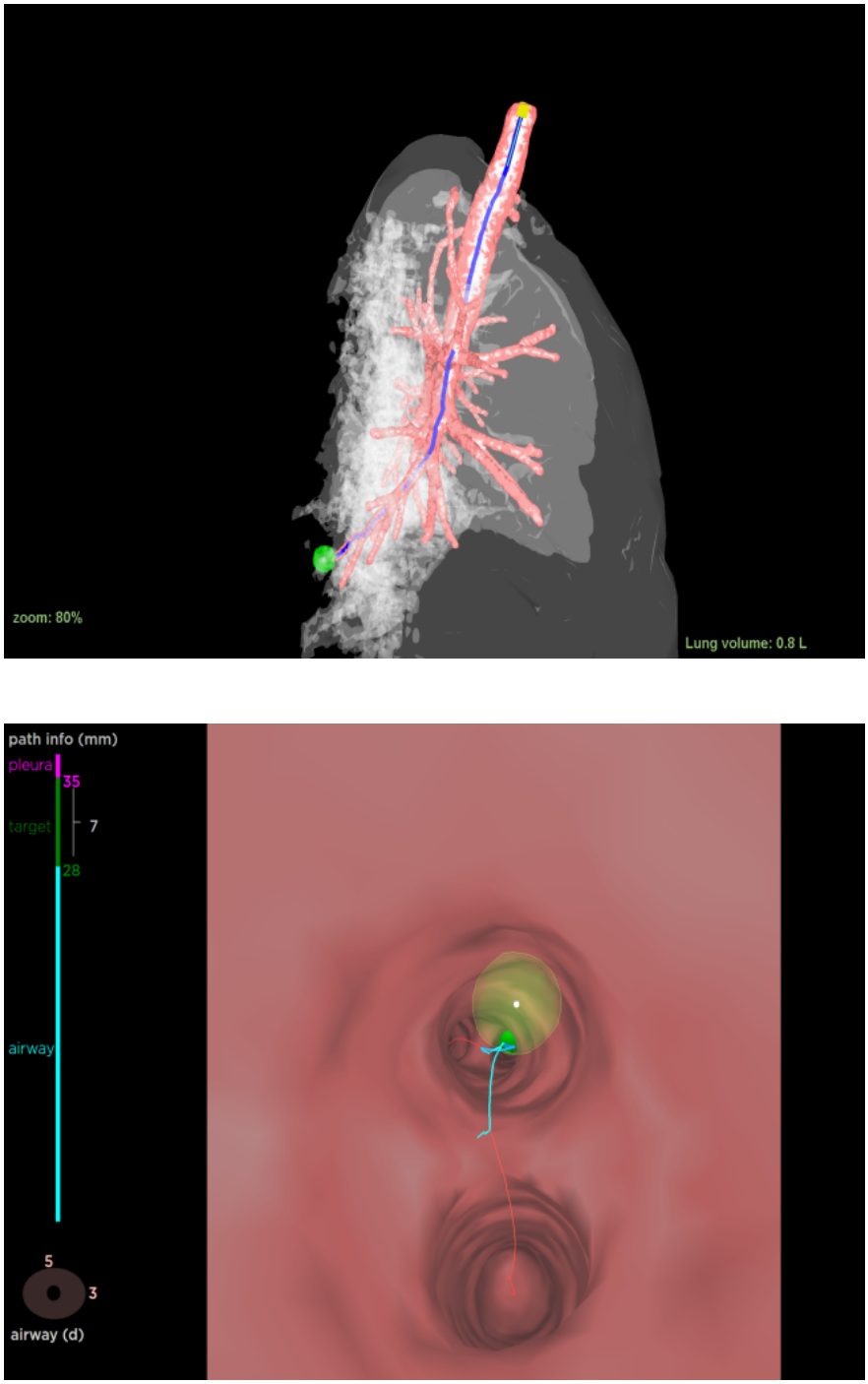


Figure 1 Preoperative planning and intraoperative guidance for virtual bronchoscopy navigation

(A, B) The virtual bronchoscopy navigation guidance pathway. (C) Intraoperative bronchoscopy guidance image for biopsy.

Figure 2

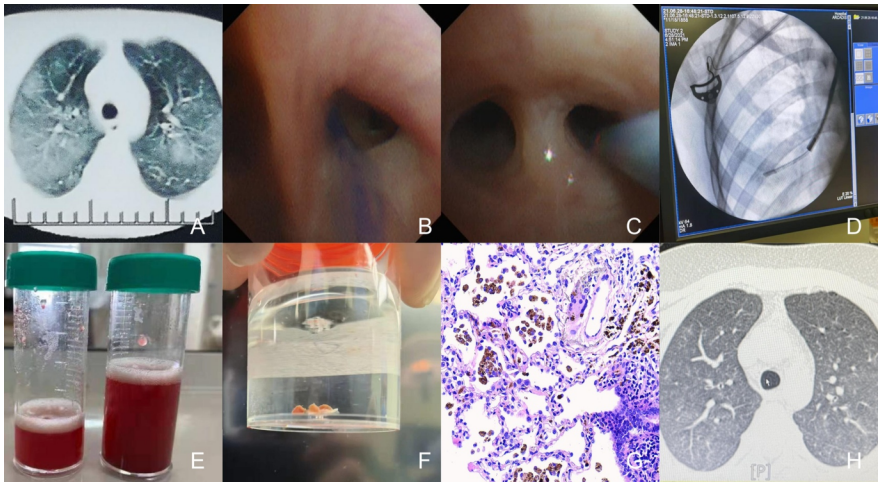


Figure 2 Chest CT, intraoperative cryobiopsy, specimen, and pathological images of child undergoing a transbronchial lung cryobiopsy.

(A) Preoperative lung CT of a child undergoing a transbronchial lung cryobiopsy. (B) Preset occlusion balloon before intraoperative biopsy and (C) during transbronchial lung cryobiopsy. (D) Confirmation of cryoprobe position by C-arm X-ray fluoroscopy. (E) Bronchoalveolar lavage fluid. (F) Frozen biopsy specimen. (G) Histopathology of biopsy specimen (HE, ×400). (H) Review of lung CT after three months of treatment.