# Application of treatment planning system assisted large-aperture computed tomography simulator in percutaneous biopsy: initial experience by a radiation therapist

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**Research**

**Keywords:** treatment planning system assisted, percutaneous biopsy, computed tomography simulator guided, puncture accuracy

**Posted Date:** March 20th, 2020

**DOI:** https://doi.org/10.21203/rs.3.rs-17977/v1

# Abstract

Background and purpose To evaluate the application of treatment planning system (TPS) assisted large-aperture computed tomography (CT) simulator in percutaneous biopsy, and report our initial experience of the accuracy and safety of this procedure.

Methods From November 2018 to December 2019, treatment planning system assisted large-aperture CT simulator guided percutaneous biopsy was performed on 38 cases, with 34 of percutaneous lung biopsy, three of abdominal lesions biopsy, and one case of deep supraclavicular lymph node biopsy. The major results including planned and actual puncture parameters, the success rate, pathological information and complications were recorded. The analyses of puncture accuracy were accomplished by pared-t test and Wilcoxon rank sum test. And the risk factors of puncture accuracy and complications were further identified.

Results The entire cohort achieved one-time success of biopsy. No significant differences were presented between planned and actual puncture depth and direction ($P = 0.436$ and $0.382$), indicating the precision of the process. And the pulmonary puncture location was related to the accuracy of puncture direction ($P = 0.033$). Biopsy specimens were successfully obtained in 38 cases. The diagnostic rate of malignancy was 76%, of which 80% for initial treatment group and 69% for treated group, respectively. For patients with pulmonary biopsy, 12 had minor pneumothorax and 2 progressed to massive pneumothorax. Only three cases suffered needle track bleeding, and no other complications were observed. Additionally, the regression analysis found a significant correlation between puncture angle and the incidence of pneumothorax ($P = 0.027$).

Conclusions TPS assisted large-aperture CT simulator improved the procedure of percutaneous biopsy by combining the advantages of radiotherapy specialty. The initial results suggested the increase of puncture accuracy and success rate, with satisfactory safety simultaneously. It might offer new insights into the field of CT-guided percutaneous biopsy.


# Introduction

As the standard for tumor diagnosis, pathological results provide vital clues for qualitative diagnosis, treatment guidance and prognostic evaluation. The computed tomography-guided (CT-guided) percutaneous biopsy, which has been extensively used in pulmonary and abdominal lesions clinically, plays an important role in obtaining tissue samples and precise pathological diagnosis. Recently, a considerable literature has grown up around the theme of improving the accuracy and efficiency in puncture process, through the application of puncture site-down positioning technique, automatic path proposal computation, or large-core needles [1–3]. Nevertheless, several major issues such as inaccurate positioning, repeated adjustment of puncture route, and the risk of serious complications after operation still remain unresolved.

Considering the CT-guided percutaneous biopsy was generally performed by interventional radiologists or thoracic surgeon previously, the present research aims to exploit the advantages of radiotherapy simulator and treatment planning system (TPS) in the department of radiation oncology to compensating the technical defects. Since 2018, we have explored the clinical application of treatment planning system assisted large-aperture CT simulator in percutaneous biopsy. Initial experience has been summarized as follows, with a view to offer new insights into improvement of puncture operation and biopsy accuracy.

# Methods And Materials

## Patients

From November 2018 to December 2019, a total of 38 patients undergoing treatment planning system assisted large-aperture CT simulator guided percutaneous biopsy at our institute were enrolled. Inclusion criteria were as follows: (1) initial diagnosed unconfirmed lesions, or treated cases in demand for pathology information again for further treatment guidance; (2) with available puncture path; (3) generally good, KPS $\geq$ 70, tolerable to puncture. Exclusion criteria were as follows: (1) poor general condition or cachexia, KPS <70, intolerable to puncture; (2) coagulation dysfunction with hemorrhagic tendency; (3) severe cardiocerebrovascular disease; (4) severe infection; (5) superficial lesions can obtain tissue specimens without imaging or B ultrasound guided puncture; (6) compulsive position due to spinal disease or other reasons.

Median age of the cohort was 62 years old (range, 32-87 years old), including 25 males and 13 females. The percutaneous lung biopsy was performed to 34 cases, abdominal lesions biopsy was performed to 3 cases (including liver, pancreas and adrenal gland), and one case of deep supraclavicular lymph node biopsy. Most of them were solid lesions. Median maximum diameter of the lesions was 3.8 cm (range, 1.1-10.1cm). Overall characteristics are outlined in Table 1. This study was approved by the Ethics Committee of Fujian Medical University Xiamen Humanity Hospital (No.XMHA2020004), in accordance with the Helsinki Declaration.

Table 1. Characteristics of 38 cases enrolled

| Characteristics | Number of cases(%) |
|---|---|
| Gender | |
| Male | 25(66) |
| Female | 13(34) |
| Age | |
| Median age | 62(32-87)years old |
| Puncture purpose | |
| Initial unconfirmed | 25(66) |
| Therapeutic evaluation | 8 (21) |
| Gene detection after PD | 5 (13) |
| Lesion location | |
| Superior lobe of left lung | 11(29) |
| Inferior lobe of left lung | 6 (16) |
| Superior lobe of right lung | 10(26) |
| Middle lobe of right lung | 4 (10) |
| Inferior lobe of right lung | 2 (5) |
| Left pleura | 1 (3) |
| Right supraclavicular lymph node | 1 (3) |
| Abdomen (liver, pancreas and adrenal gland) | 3 (8) |
| Lesion character | |
| Solid | 36(94) |
| Frosted glass | 1 (3) |
| Solid-cystic | 1 (3) |
| Maximum diameter | |
| Median maximum diameter | 3.8(1.1-10.1)cm |

Abbreviations: PD = Progression Disease

## Process

### Puncture procedures

(1) Preoperative preparation: air sterilization of the CT simulator room, confirmation of the puncture supplies and rescue medicines, and measurement of life indications for patients.

(2) Instrument and equipment: Philip 16-multislice spiral large-aperture CT simulator along with movable three-dimensional laser positioning system, immobilization device (vacuum fixation mat or prone board), Eclipse 13.5 planning system, and Bard 17G coaxial biopsy needle.

(3) Immobilization and CT scan: the optimum position was selected for patients according to the location of target lesions, and vacuum fixation mat or prone board were applied for fixing the patients in their comfortable positions. Then, select the location points and paste spherical metal markers on patients' surface. Mark cross lines according to the laser line, and draw extension lines on the vacuum fixation mat or prone immobilization device to determine the relative position. Location point-centered CT scan was performed with layer thickness of 3 mm subsequently, and the images were transmitted to the radiotherapy server.

(4) Determination of puncture path: CT images were imported into Varian TPS and the origin was set on TPS. To design the optimum puncture path, take the maximum cross-section level of the target lesion as possible, avoid bones and great vessels, and pierce normal tissue as few as possible. The puncture target (named GTV) was delineated by the radiation therapist, and a new Plan was created by the radiotherapy physicist according to the planned path. Subsequently, the source skin distance was changed to 100 cm (SSD = 100 cm), and the relative coordinates (X, Y, and Z values) of the location point and the puncture point were recorded. Puncture direction and depth were recorded meanwhile. With the assist of the laser

positioning system, the puncture point based on the relative coordinates was accurately located onto the surface of the patient. The above operations were checked by two technicians.

(5) Verification of puncture point: puncture point was marked and axial scan was performed to verify the location of puncture point, avoiding set-up error as well.

(6) Percutaneous biopsy: After routine sterilization and local anesthesia, the coaxial biopsy needle punctured into the proximal region of lesion based on the planned direction and depth (calibrated by laser line and protractor). And the location of biopsy needle would be verified by CT scan then (for adjustment if necessary). Two or three satisfactory specimens were collected into specimen bottle with formalin and sent for pathological examination. The skin of puncture region was disinfected and bound up postoperatively, and CT scan of the puncture site and adjacent area was performed to confirm whether there were signs of pneumothorax and bleeding. Close observation for 6 hours was required for each patient. The workflow was shown in Figure 1.

### Outcome measures

The planned and actual puncture direction and depth were recorded for comparison separately. $\Delta H$ was defined as the difference between the planned and actual puncture depth, and $\Delta \alpha$ was defined as the difference between the planned and actual puncture direction. Another indexes included puncture time, frequency of needle adjustment, pathological results and complications.

### Statistical analysis

The parameters of puncture accuracy were analyzed using pared-t test and Wilcoxon rank sum test. The regression analysis was adopted to identify the risk factors of puncture complications. All statistical analyses were performed by IBM SPSS version 23.0, Chicago, USA, and the workflow was drawn by Microsoft Visio 2019, Washington, USA. Any difference was considered to be statistically significant if p was $< 0.05$.

## Results

### Puncture accuracy

Puncture time for each case was within 20 minutes. The entire cohort achieved one-time success of biopsy. Thirty-four patients had CT scans 4 times, while the remaining 4 underwent one more time due to slight deviations adjustment. Strong evidence was found when the actual puncture depths were close to the planned ones. And there was no significant difference between the planned and actual puncture depth (5.34 ± 2.01cm vs. 5.28 ± 1.95cm, $t = 0.788$, $P = 0.436$). The average deviation of depth $|\Delta H|$ was 0.37 ± 0.32cm, which indicated the precision of the puncture depth. As regard to the puncture direction, the median planned and actual angles were 90 ° and 88 ° respectively, without statistically significant difference between them either ($z = -0.873$, $P = 0.382$), demonstrating the high consistency. Specific results are presented in Table 2.

Table 2. Puncture accuracy in 38 cases（$\bar{x}$±s / M)

| Parameter | Planned | Actual | t/z | P |
|---|---|---|---|---|
| Puncture depth | 5.34±2.01cm | 5.28±1.95cm | 0.788 | 0.436 |
| Puncture angle | 90° | 88° | -0.873 | 0.382 |

It was apparent from Table 3 that the deviations in puncture depth and angles were well controlled regardless of the size and location of lesions.

Although no significant differences were detected in puncture accuracy between different lesion size subgroups (P = 0.712, P = 0.744), it can be seen that |ΔH| tended to decrease with the increase of lesion size. In addition, |Δα| in the upper lobe of lung was significantly smaller than that in the middle and lower lobe ($\chi^2$ = -2.129, P = 0.033), suggesting the pulmonary puncture location had an effect on the accuracy of puncture direction. Figure 2 and Figure 3 illustrate examples of percutaneous pulmonary puncture.

Table 3. The effect of lesion size and puncture location on puncture accuracy（$\bar{x}$±s）

| Variable | \|ΔH\| | Z/$X^2$ | P | \|Δα\| | Z/$X^2$ | P |
|---|---|---|---|---|---|---|
| Lesion size | | 0.680 | 0.712 | | 0.590 | 0.744 |
| ≤3cm（n=13） | 0.40±0.33cm | | | 3.77±3.49° | | |
| 3-5cm（n=19） | 0.35±0.30cm | | | 3.63±3.53° | | |
| ＞5cm（n=6） | 0.33±0.40cm | | | 6.33±6.89° | | |
| Puncture location | | -0.599 | 0.549 | | -2.129 | 0.033 |
| Superior lobe of lung（n=21） | 0.34±0.27cm | | | 2.62±3.02° | | |
| Middle and inferior lobe（n=12） | 0.46±0.41cm | | | 5.42±3.80° | | |

## Pathological results

Biopsy specimens were successfully obtained in 38 cases. The success rate of puncture was 100%. As summarized in Table 4, diagnostic rate of malignancy was 76% (29/38), of which 80% (20/25) for initial treatment group and 69% (9/13) for treated group, respectively. Among 29 malignant tumor cases, adenocarcinoma was confirmed in 16 cases, squamous cell carcinoma in 6 cases, small cell carcinoma in 2 cases, metastatic disease in 3 cases, and the rest malignant tumor typing could not be further identified by immunohistochemistry due to insufficient specimens. The other 9 cases were diagnosed as benign disease.

Table 4. Pathological results of 38 cases

| Pathological results | Number of cases（%） |
|---|---|
| Adenocarcinoma | 16（42） |
| Squamous cell carcinoma | 6（16） |
| Small cell lung cancer | 2（5） |
| Metastatic sarcoma | 2（5） |
| Metastatic hepatocellular carcinoma | 1（3） |
| Malignant epithelial carcinoma | 2（5） |
| Inflammation | 7（18） |
| No malignancy | 2（5） |

## Complications

Minor needle track bleeding was observed in 3 cases. For patients with pulmonary biopsy, 12 had minor pneumothorax (12/33, 36%), of which 2 progressed to massive pneumothorax by reexamination after 24-48 hours, (2/33, 6%). Patients with massive pneumothorax were cured after closed thoracic drainage, and minor pneumothorax were absorbed themselves without intervention. No other complications such as hemoptysis, hemothorax or subcutaneous hematoma were found in the cohort. Moreover, no puncture-related complications such as bleeding, infection, and pancreatitis were observed in 3 patients with abdominal biopsy.

Based on further regression analysis, a significant correlation was found between puncture angle and pneumothorax. Incidence rate of pneumothorax in puncture with 80-100° was significantly higher than that with other angles (48% vs. 10%, P = 0.027). However, age, lesion size, lesion location, and puncture depth had no effect on pneumothorax (P＞0.05). But there was still a tendency that patients with aged ≥ 65 years or puncture depth ≥ 5 cm were more susceptible to pneumothorax. The effects of variables on pneumothorax are shown in Table 5.

Table 5. Regression analysis of factors affecting the incidence of pneumothorax

| Variable | Pneumothorax/No pneumothorax | P |
|---|---|---|
| Gender | | 0.198 |
| Male（n=21） | 9/1 | |
| Female（n=12） | 3/9 | |
| Age | | 0.278 |
| ≥65 years old（n=17） | 8/9 | |
| ＜65 years old（n=16） | 4/12 | |
| Puncture purpose | | 0.356 |
| Initial treatment（n=22） | 9/13 | |
| Treated（n=11） | 3/8 | |
| Lesion location | | 0.183 |
| Superior lobe of lung（n=21） | 7/14 | |
| Middle and inferior lobe（n=12） | 5/7 | |
| Lesion size | | 0.829 |
| ≤3cm（n=4） | 2/2 | |
| 3-5cm（n=16） | 5/11 | |
| ＞5cm（n=13） | 5/8 | |
| Puncture depth | | 0.607 |
| ≥5cm（n=18） | 7/11 | |
| ＜5cm（n=15） | 5/10 | |
| Puncture angle | | 0.027 |
| 80-100°（n=23） | 11/12 | |
| ＜80° or ＞100°（n=10） | 1/9 | |
| Needle adjustment | | 0.735 |
| Once（n=4） | 1/3 | |
| No（n=29） | 11/18 | |

# Discussion

In the era of individualized precision treatment, especially with the advancement of molecular targeted therapy and immunotherapy, pathology is prerequisite for further gene detection, exploration of drug resistance mechanisms, and evaluation of patients’ conditions [4–6]. CT-guided percutaneous biopsy, as one of the important solution for pathological information acquisition, is playing a more critical role in clinical practice [7], which requires better operability and accuracy. Yet, there still exist defect in inaccurate positioning, low one-time success rate, heterogeneity of operators’

experience, and the poor compliance of some patients who are prone to serious complications. This is the first study to combine TPS and radiotherapy positioning system into the puncture process, which has refined the operation. The initial results suggested the advantages of puncture accuracy and higher success rate, with satisfactory safety simultaneously. It might make an important contribution to the field of CT-guided percutaneous biopsy.

The advantages of involving TPS in CT-guided percutaneous biopsy are summarized as follows: the pre-puncture area (defined as GTV) could be freely delineated by operators on TPS according to their clinical experience and imaging features of lesions, avoiding the region of tumor liquefaction or necrosis, and improving the detection rate ultimately. Furthermore, with the accurate coordinate information conversion between TPS and CT simulator system, the optimal puncture point would be projected to patients' surface based on the relative coordinate, which is accurate to the millimeter. Therefore the accuracy of positioning is greatly improved compared with the traditional method of using a standard lead point mesh, and the restriction on the choice of puncture point is reduced to a certain extent.

Several attempts had been made to improve the puncture accuracy [8, 9], but they didn't taken inevitable errors between actual operations and ideal presets into account. Herein, we compared the actual and planned puncture data. The results showed a good agreement in them. There was no statistical difference between actual and planned puncture depth (5.28 ± 1.95 cm vs. 5.34 ± 2.01 cm, $P = 0.436$) and angles (88 ° vs.90 °, $P = 0.382$). The reason why actual puncture depth was less than the planned one might be different levels of skin retraction during puncture. Ultimately, the deviations were controlled within the satisfactory range, and the one-time success rate reached 100%, manifesting this technology was eligible for clinical application.

Puncture accuracy is thought to be associated with detection rate, and it is influenced by multiple variables. Tsukada et al. [10] reported 123 patients with pulmonary nodules, and found that diagnostic accuracy decreased in proportion to the decrease in lesion size. Kothary et al. [11] also drew a conclusion that diagnostic accuracy of CT-guided percutaneous lung biopsy of lung nodules ≤ 1.5 cm was lower than that of nodules > 1.5 cm. In our study, detection rate was 100%. Diagnosis rate of malignancy was 76% in the cohort and 80% in initial treatment patients, which was slightly higher than recent literature reports [8]. Although lesion size showed no remarkable effect on puncture accuracy, $|\Delta H|$ tended to decrease with the increase of lesion size. Additionally, pulmonary puncture location was found to be the risk factor of the puncture direction accuracy ($P = 0.033$). This might be caused by the difference of respiratory mobilities between different lung lobes, which affected the operator's control of the puncture direction. But generally the deviation was well controlled within 10 °. Ji et al. [8] stated that 3D printed planar template could better achieve unbiased needle insertion. Nevertheless, it required multiple invasive fixation needles during operation, and lacked advantages in frequency of CT scans and operation duration. By contrast, the method applied in present research has simplified the puncture process and improved the success rate on the basis of ensuring the puncture accuracy, with certain advantages in puncture efficiency and frequency of CT scans compared to 3–6 times CT scans reported in previous literatures [8, 12].

The most common complication of pulmonary puncture reported was pneumothorax, followed by hemorrhage, but there was no consensus on the incidence rate. Most of pneumothorax rates were between 5.3% and 42%, of which the incidence of closed thoracic drainage required was about 2%-21%. The incidence of pulmonary hemorrhage was 5%-30%, and severe pulmonary hemorrhage accounted for 3.1% [13–16]. This study showed 36% of minor pneumothorax rate, and 6% progressed to massive pneumothorax. Only three cases suffered needle track bleeding, and no other rare complications were observed. The complication rates were consistent with previous studies, and pulmonary hemorrhage seemed to occur less. The improvement of positioning accuracy and patients' comfort might contribute to it. High one-time success rate also helped to avoid lung tissue and vessels damage caused by repeated needle adjustment. Some researchers believed that small lesions and repeated puncture had prognostic value for pneumothorax [17]. Yin et al. [18] also stated that pneumothorax was associated with the lesion size and depth of needle penetration. Our further investigation revealed puncture direction was the risk factor of pneumothorax, but age, lesion location, lesion size and puncture depth had no effect on it. This might be related to insufficient sample size of this study. For this cohort, the occurrence of complications was less affected by clinically relevant factors, which reflected the safety of this technology to some extent. Yet, it is still need to be verified by a larger sample research in the future.

Similar to other preliminary studies, some limitations are unavoidable. We have enrolled all 38 eligible cases in our institution and evaluated them as thoroughly as possible. But a more comprehensive analysis was still restricted by small sample size when identifying risk factors of puncture accuracy and complications. For small lesions with high puncture difficulty, it will be more convincing if subgroup analysis is performed on the basis of enlarged sample to verify the technical superiority. In addition, abdominal cases were very limited, making it hard to explore more details in this subgroup. Further investigation is needed.

Synthetically, this study summarized the initial experience and results of clinical application of TPS assisted large-aperture CT simulator guided percutaneous biopsy to improve the procedure by combining the advantages of radiotherapy specialty. The emerging technology enhanced the puncture accuracy and success rate under the premise of ensuring safety and efficiency, which is worth promoting in clinical application.

# Abbreviations

TPS treatment planning system

CT computed tomography

CT-guided computed tomography-guided

SSD source skin distance

PD Progression Disease

# Declarations

## Acknowledgements

We are grateful to our colleagues from department of oncology and surgical oncology who provided expertise that greatly assisted the research. We also have to express our immense appreciation to Professor Jiade Lu for sharing his pearls of wisdom and his comments on an earlier versions of the manuscript.

## Funding

This study was supported by the Fujian Provence Natural Science Foundation No. 2018 J01266. It played an role in the design of the study, interpretation of data and in writing the manuscript.

## Contributions

XYL, YQL, and XQK designed the study. XYL, SYL, and JQH analyzed and interpreted the patient data regarding the pathological and clinical outcome. XYL and YLD performed the statistical analysis. XYL wrote the manuscript. All authors read and approved the final manuscript.

## Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of Fujian Medical University Xiamen Humanity Hospital (No.XMHA2020004), in accordance with the Helsinki Declaration.

## Consent for publication

The consent for publication was obtained from the patient whose images were contained in the final manuscript.

## Conflicts of Interest

The authors have declared that no competing interests exist.

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## Figures

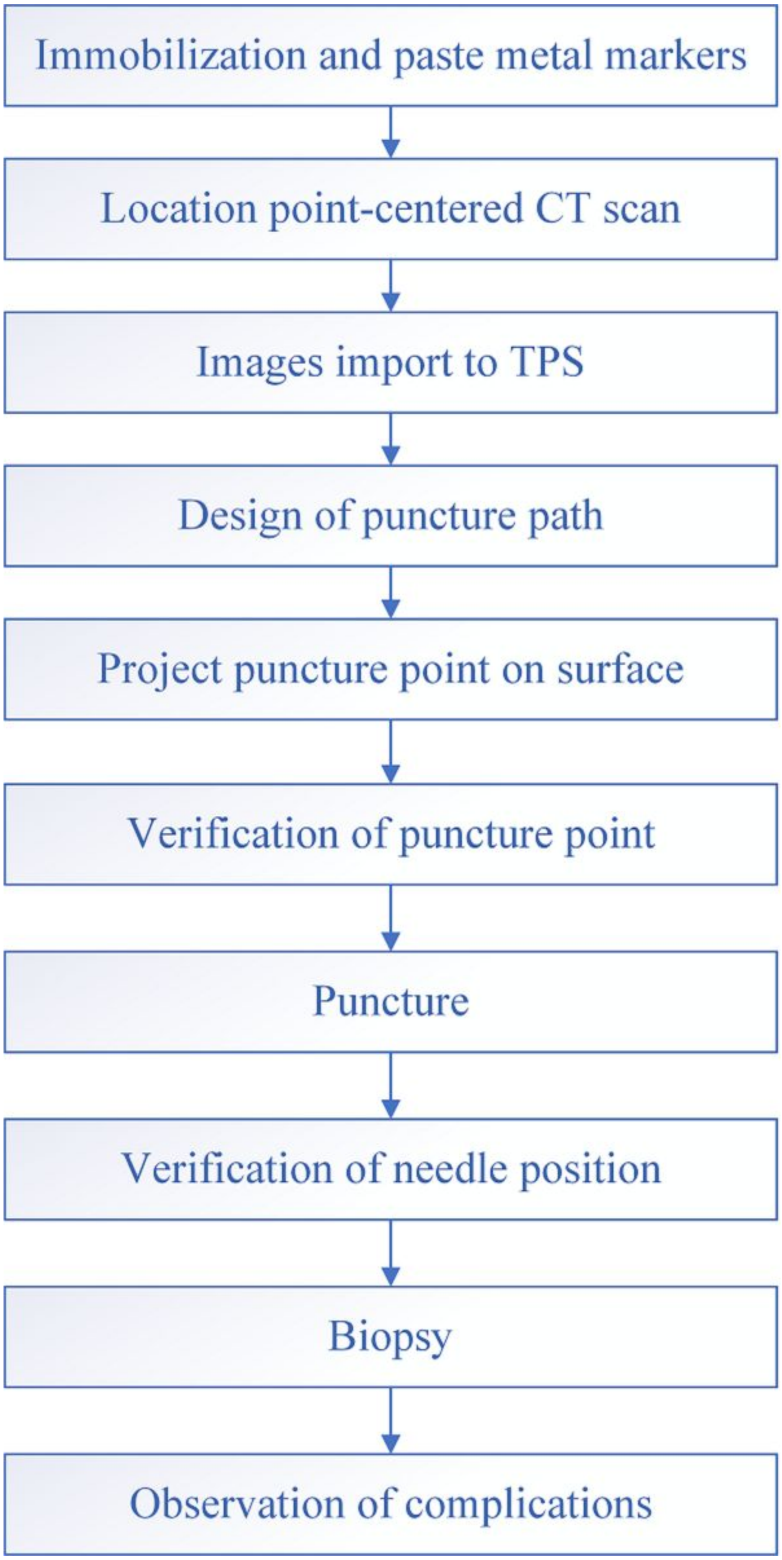
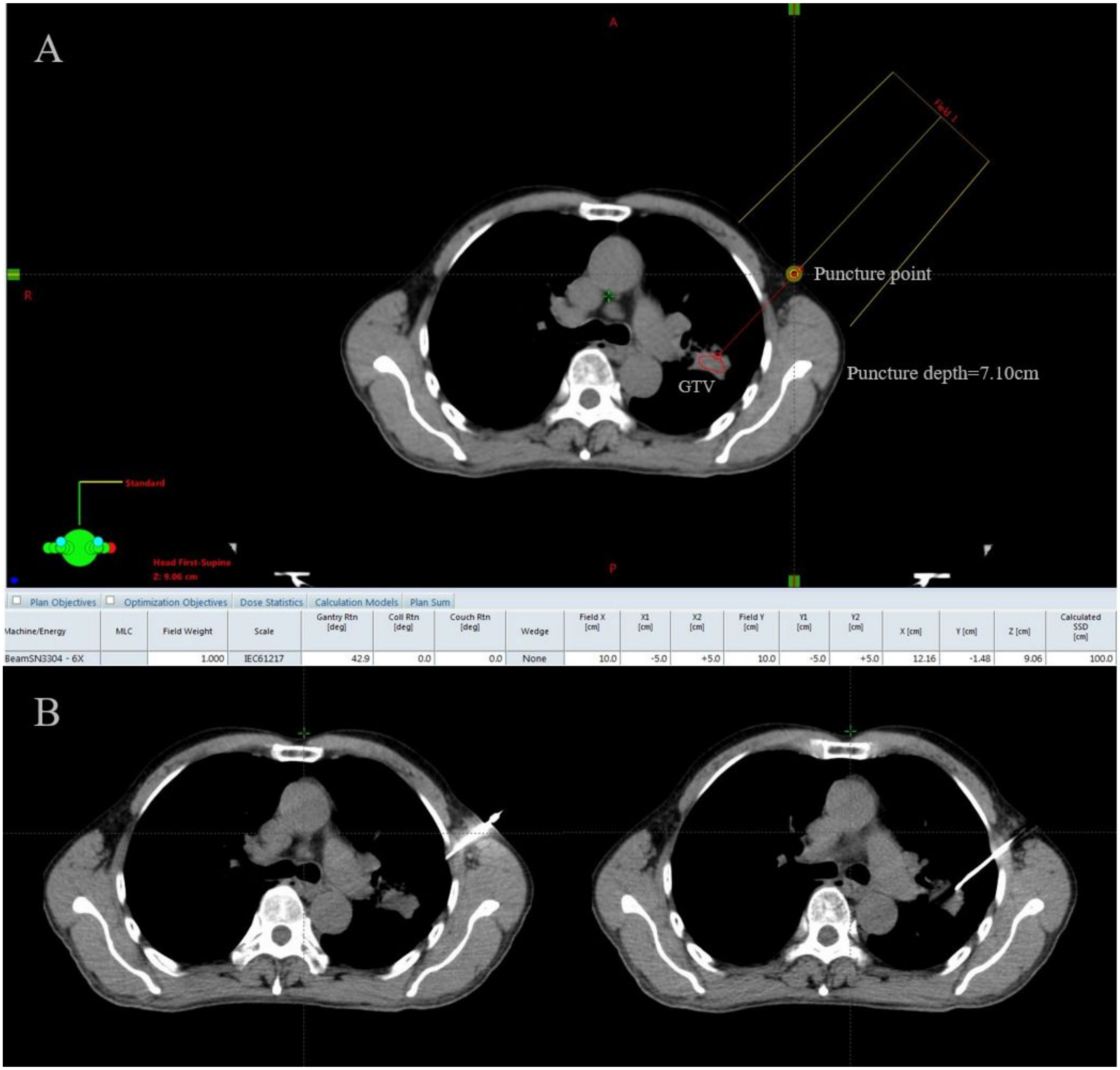



**Figure 1**

Flow diagram of treatment planning system assisted large-aperture CT simulator guided percutaneous biopsy.




| Machine/Energy | MLC | Field Weight | Scale | Gantry Rtn [deg] | Coll Rtn [deg] | Couch Rtn [deg] | Wedge | Field X [cm] | X1 [cm] | X2 [cm] | Field Y [cm] | Y1 [cm] | Y2 [cm] | X [cm] | Y [cm] | Z [cm] | Calculated SSD [cm] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BeamSN3304 - 6X | | 1.000 | IEC61217 | 42.9 | 0.0 | 0.0 | None | 10.0 | -5.0 | +5.0 | 10.0 | -5.0 | +5.0 | 12.16 | -1.48 | 9.06 | 100.0 |

## Figure 2

Illustration of an example. (A) A Plan was created on TPS to design the optimum puncture path. The relative coordinates (X, Y, and Z values) were generated automatically when puncture point was determined. (B) The position of biopsy needle was verified.

**Figure 3**

Illustration of positioning. With the help of the laser positioning system, puncture point based on the relative coordinates was accurately located onto the surface of the patient.