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Comparison of the harvest volume between maneuvers of endobronchial ultrasound-guided transbronchial needle aspiration including the "cross-fanning technique"

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Abstract

Recently, a certain volume of biopsy specimens has been required for genetic testing of tumors using endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). This study aimed to verify the superiority of our newly devised EBUS-TBNA biopsy technique, the "cross-fanning technique," which combines rotation and up-down maneuvers, by comparing its harvest volume with that of other maneuvers. Using a bronchoscope simulator, ultrasonic bronchoscope, and 21-gauge puncture needle, we compared the weight of silicone biopsy specimens obtained by the following 4 procedures: Conventional maneuver; Up-down maneuver; Rotation maneuver, and; Cross-fanning technique. Each procedure was repeated 24 times in total, rotating the sequences of the maneuvers, and the operator/assistant pair to align the conditions. The means ± standard deviations of the sample volumes for each puncture technique were as follows: 2.8 ± 1.2 mg; 3.1 ± 1.6 mg; 3.7 ± 1.2 mg, and; 3.9 ± 1.2 mg. There was a significant difference between the 4 groups ($P = .024$). The post hoc test showed a statistically significant difference between techniques A and D ($P = .019$). This study showed that the cross-fanning technique might contribute to the increased volume of tissue samples obtained by EBUS-TBNA biopsy.

Abbreviations: EBUS-TBNA = endobronchial ultrasound-guided transbronchial needle aspiration, EBUS = endobronchial ultrasound.

Keywords: biopsy needle, endobronchial ultrasound-guided transbronchial needle aspiration, fanning, puncture technique, sample volume

1. Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was developed by Yasufuku et al[1–4] and is now widely used as a biopsy procedure for the diagnosis of lesions adjacent to the trachea or central bronchi, and for the staging of malignancy. Recently, with progress in molecular analysis, the role of EBUS-TBNA has evolved from a primarily diagnostic and staging modality for managing lung cancer to one of the main techniques for obtaining tumor samples for molecular testing for genetic analyses and predictive biomarkers testing.[5,6] With this change in the role of EBUS-TBNA, the primary focus has been changing from diagnostic yield to cellular quality and quantity, which has increased the procedure's technical demands.[6] A higher tumor cell abundance has been associated with a higher DNA yield, but more needle passes do not necessarily yield more DNA.[7] Few studies have showed the difference in specimen volume yield according to harvest maneuvers. In endoscopic ultrasound-fine needle aspiration for pancreatic lesions, the efficacy of the fanning technique has been reported, which changes the puncture direction of the biopsy needle by an up-down maneuver of the scope.[8] A randomized trial of endoscopic ultrasound-fine needle aspiration showed that there was a significant difference in the total number of passes required to establish the diagnosis between the standard (N = 26) and fanning cohorts (N = 28) (median 1 [IQR 1–3] vs 1 [IQR 1–1]; $P = .02$), respectively (primary outcome), though there was no significant difference in diagnostic accuracy between the fanning and standard techniques (96.4% and 76.9 %, respectively; $P = .05$) (secondary outcome). This indicates the possibility of obtaining the specimen needed for diagnosis with fewer passes with the fanning technique. In addition, it showed that no complications or technical failures (needle dysfunction) were observed with the fanning technique.[8] We suspect that the efficacy of the fanning technique might be derived from the enlargement of the harvest area by expanding the linear harvest area (1-dimensional) (Fig. 1A) to the

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

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plane area (2-dimensional) (Fig. 1B). Similarly, we expected that by adding the rotation movement (Fig. 1C), we would be able to change the 2-dimensional harvest area to a 3-dimensional area, increasing the specimen yield. Therefore, we devised a technique to change the puncture direction of the biopsy needle by both an up-down and rotation maneuver of the scope (we named this technique as "cross-fanning technique" in this report) (Fig. 1D) and used it to conduct an EBUS-TBNA biopsy since 2012 with a favorable impression to increase sample volume compared to conventional techniques. In our earlier study where we used the rotating and up-down maneuver in some cases, we reported the histological diagnostic sensitivity of sarcoidosis by EBUS-TBNA to be 92.9% (39/42).[9] However, until now, there is no literature to support harvest technique on specimen yield. It has not been verified whether this technique can obtain a larger volume of specimens than the conventional method. Hence, we conducted experimental tests to compare the sample volumes obtained by each harvest technique using EBUS-TBNA. In this study, we aimed to assess if a cross-fanning technique has the potential to improve diagnostic specimen yield by comparing the cross-fanning technique to other maneuvers utilizing a silicone model.

2. Methods

2.1. Institutional review board approval

This study was approved by the institutional review board of the National Hospital Organization Himeji Medical Center (registration number 04-05).

2.2. Experiment

Using an ultrasonic bronchoscopy simulator (LM-099; Koken Ltd., Tokyo, Japan), a target model (LM-099A; Koken Ltd.) made of silicon rubber, an ultrasonic bronchoscope (BF-UC290F; Olympus Corp., Tokyo, Japan), and a 21-gauge EBUS-TBNA needle (ViziShot2, NA-U401SX; Olympus Corp.), we harvested the silicone specimens by puncturing the spherical hypoechoic part of the target model placed in front of the simulated trachea. After piercing the EBUS-TBNA needle into the target model, the stylet was pushed once and pulled out from the needle.

Thirty needle passes were performed for each harvesting technique. The suction pressure was – 20 mL. A metronome was used to maintain a constant puncture speed, and 1 puncture was performed once every 2 seconds (30 needle passes per minute). An assistant performed needle movement for puncture. The needle passes were performed for each harvest maneuver as follows (Fig. 1A–D). A: Conventional maneuver, 30 needle passes in the same direction; B: up-down maneuver, 5 needle passes in the up position, 5 needle passes in the neutral position, and 5 needle passes in the down position × 2 sets; C: rotation maneuver, 5 needle passes in the left rotation position (Fig. 1A–C), 5 needle passes in the front position (Fig. 1B and C), and 5 needle passes in the right rotation position (Fig. 1C) × 2 sets; and D: cross-fanning technique, 1 set of the rotation maneuver and 1 set of the up-down maneuver as described above.

In the rotation maneuver, the rotation angle was approximately 45° (Fig. 1C and D). The 4 harvest maneuvers were performed in series (1 course). The target was replaced for each course as the result might be affected if a previous puncture damaged the silicone structure. The puncture needle was also exchanged for each course to avoid degradation of puncture quality due to repeated punctures. To ensure equal conditions for each harvest maneuver, 4 courses were conducted in which the sequences of the harvest techniques differed as follows: A→C→B→D, C→B→D→A, B→D→A→C, and D→A→C→B.

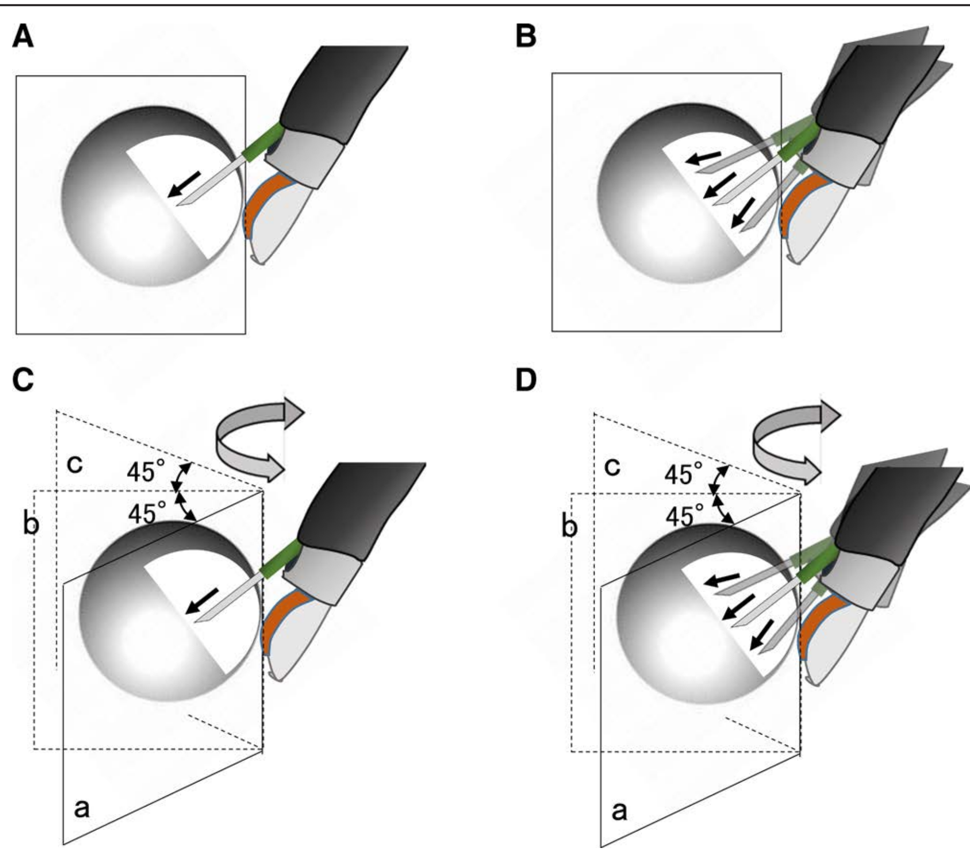

Figure 1. (A) Conventional maneuver, the biopsy needle moves back and forth linearly. (B) Up-down maneuver, the harvest area is expanded to the plane. (C) Rotation maneuver, with rotation movement of the scope. (D) Cross-fanning technique, combination of the up-down and rotation maneuvers.

An operator and assistant repeated the maneuvers. The members of the pair were fixed, and to avoid the influence of the years of experience of the operators, 2 pairs with different years of experience were included. The number of years of experience performing EBUS-TBNA was as follows: pair 1, 11 years for the operator and 5 years for the assistant, and pair 2, 4 years for the operator and 3 months for the assistant. Each pair performed the 4 courses thrice (12 courses in total for each pair).

2.3. Specimen measurement method

The specimen obtained from the silicon rubber target was extruded onto weighing paper by pushing it with a stylet, then extruded with 20 mL of air 3 times. The specimen attached to the tip of the EBUS-TBNA needle was recovered using an antistatic spatula. The sample volume was evaluated by weight and measured using an electronic analytical balance (minimum display, 0.0001 g; ATY64; Shimadzu Corporation, Kyoto, Japan) (Fig. 2A and B). Sample weights were measured in milligrams.

To avoid measurement errors due to electrostatic charge, the measurement was conducted during summer (July to August) when the humidity was high. The mean ± standard deviation temperature and humidity during the experiment were 25.5 ± 0.5°C and 68 ± 2%, respectively. This novel experimental design uses a silicone/bronchoscopic simulation model and evaluated sample yield by weight.

2.4. Statistical analysis

We investigated whether there were any significant differences between the 4 puncture techniques in the sample weights obtained with each puncture method. We also investigated whether there was a difference between the 4 puncture methods between each of the pairs. Bartlett Test was used to assess the homogeneity of variance before comparing 4 methods. A 1-way analysis of variance was used to determine if there was a statistically significant difference between the 4 puncture methods. Dunnett correction was used as a post hoc analysis. A *P* value <.05 was considered statistically significant. All statistical analyses were performed using Easy R, which is a modified version of the graphical user interface of R statistical software designed to add statistical functions frequently used in biostatistics (The R Foundation for Statistical Computing, Vienna, Austria).[10]

3. Results

The sample weights obtained for each harvest maneuver are shown in Figure 3. The average ± standard deviation of the sample yield was as follows: 2.8 ± 1.2 mg; 3.1 ± 1.6 mg; 3.7 ± 1.2 mg, and; 3.9 ± 1.2 mg. The assumption of homogeneity of variance across groups was not rejected (*P* = .423, Bartlett test). A statistically significant difference in sample weight was observed between these harvest maneuvers (*P* = .024, 1-way analysis of variance). According to the multiple comparison test, there was a statistically significant difference between the conventional and cross-fanning techniques (*P* = .019, Dunnett correction).

The sample weight evaluation for each operator pair is shown in Figure 4. The assumption of homogeneity of variance across groups was not rejected in pair 1 and pair 2 (*P* = .650, *P* = .579, respectively, Bartlett test). In pair 1, there was a statistically significant difference between 4 techniques (*P* = .048, 1-way analysis of variance) but not a statistically significant difference between the conventional and cross-fanning techniques (*P* = 0. 093, Dunnett correction). In pair 2, there was no statistically significant difference between the 4 techniques (*P* = .399, 1-way analysis of variance).

4. Discussion

This study showed that EBUS-TBNA with the cross-fanning technique might increase the specimen yield compared to the conventional maneuver. This result indicated that puncturing with multiple directions may increase sample volume. This technique is a novel approach, but can be incorporated with previously reported techniques and into practice. Several ingenuities

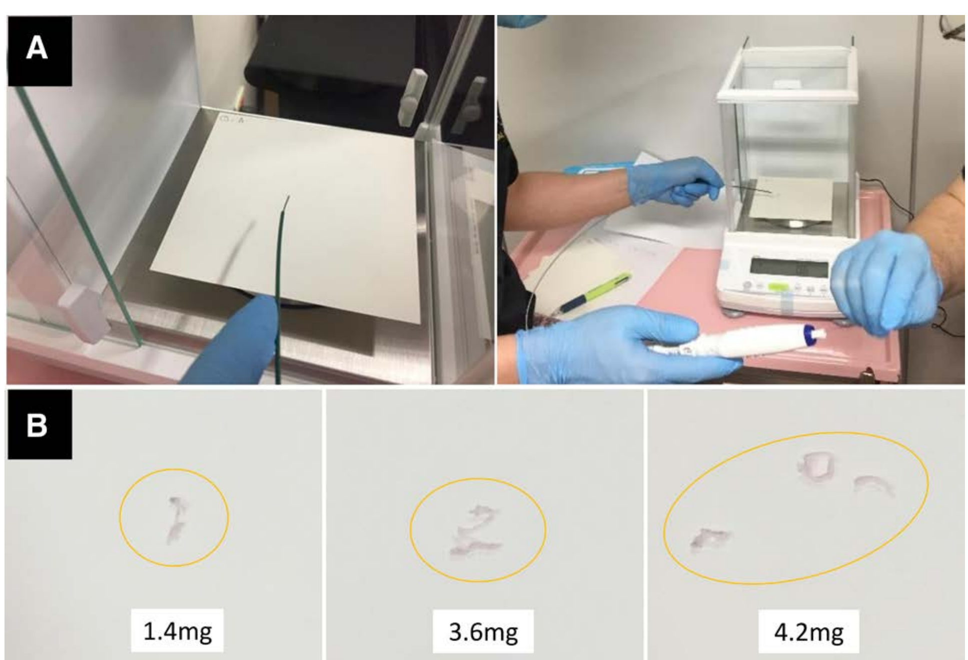

Figure 2. (A) The sample was extruded on a weighing paper with a stylet and weighed and measured using an electronic analytical balance (ATY64; Shimadzu Corporation, Kyoto, Japan). (B) Examples of silicon specimens obtained from the simulator by endobronchial ultrasound-guided transbronchial needle aspiration.

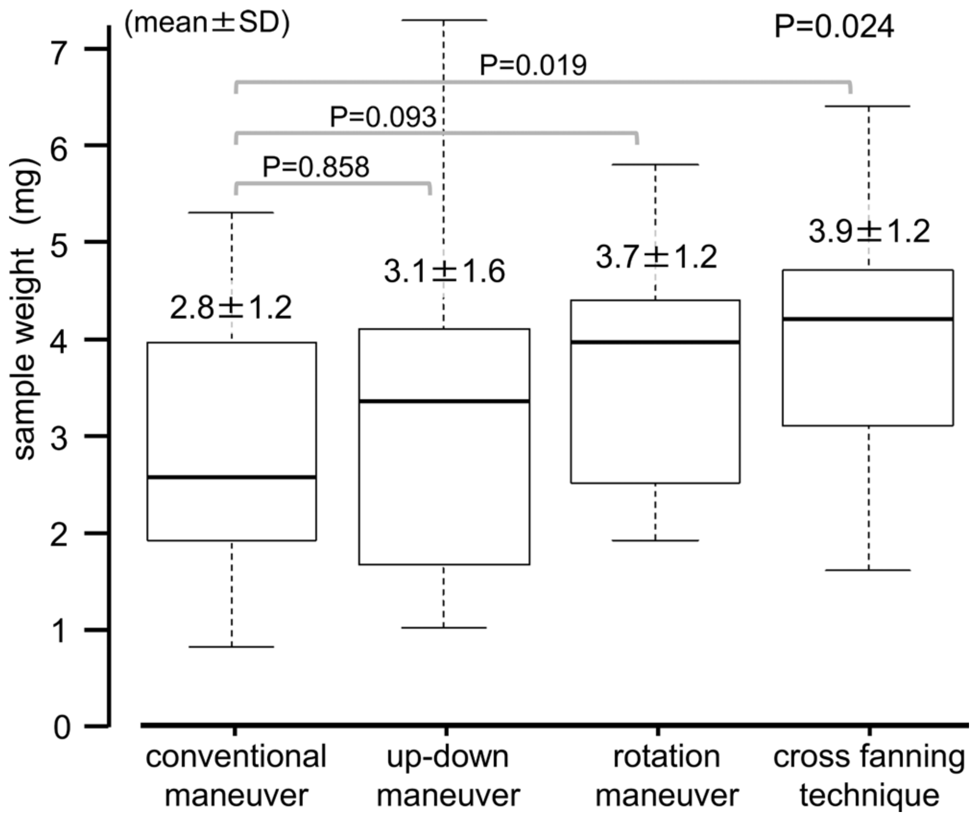

Figure 3. Comparison of the sample weights of each harvest maneuver (*P* = .0239, 1-way analysis of variance) (mean ± standard deviation). A significant difference is observed between A (conventional maneuver) and D (cross-fanning technique) (*P* = .019, Dunnett correction).

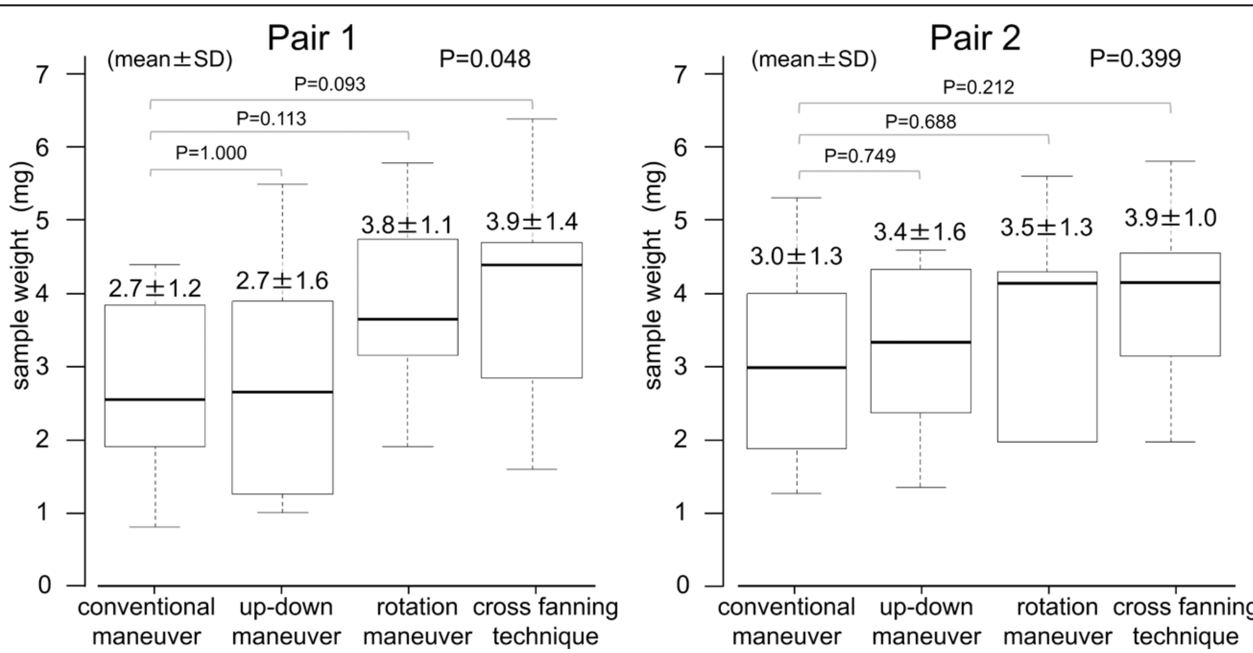

Figure 4. Comparison of the sample weight of each harvest maneuver in each operator pair.

have been made to improve the sample yield in EBUS-TBNA. Multiple EBUS-TBNA needles with different gauges (19, 21, 22, and 25),[11–17] different metal materials,[18] and different shapes[19,20] have been fabricated. The presence or absence of suction pressure,[21–23] a combination of rapid cytopathology,[24,25] and the difference of the number of the needle passes[7,26] has also been studied. However, it cannot be said that either the EBUS-TBNA puncture needles, the presence or absence of suction pressure, or what number of needle passes are superior. Therefore, the selection is based on the case.[27]

Few reports have investigated the difference in specimen yield by various harvest maneuvers under the same conditions as the EBUS-TBNA puncture needle and suction pressure. Inoue et al developed the outer sheath method and reported that it significantly improved the diagnostic yield.[28] In a study using ex vivo calf lungs (proceedings), it was reported that the sample volume increased by the fanning maneuver in EBUS-TBNA.[29]

A quantitative comparison of the amount of EBUS-TBNA harvest is not easy due to the difficulty in comparing biopsy specimens by length or volume. They are often fragmented, and blood components are contaminated if a biomaterial model is used.

In the model used herein, the sample did not contain blood, and the silicone rubber used as the lesion model consists of a uniform material. Thus, it was possible to evaluate the sample volume by weight. There was no contradiction between the measured weight of the EBUS-TBNA specimens collected from the simulator model and the gross estimation of the sample amount by the naked eye (Fig. 2B). Moreover, comparative studies are difficult due to the large dispersion of the sample volume during each puncture. However, an experiment with a simulator and a silicon rubber target resolves this problem by allowing the procedure to be repeated repeatedly under the same conditions. The significance of our study is that it revealed for the first time the difference in the amount of EBUS-TBNA specimens, which is highly variable and difficult to evaluate, depending on the puncture techniques.

Finally, our experiment revealed the cross-fanning technique's possible superiority over the conventional maneuver. We could not clarify the superiority of this technique compared to the rotation or up-down maneuvers; however, these 2 maneuvers did not significantly differ from the conventional maneuvers. This finding supports the advantage of the cross-fanning technique.

Additionally, although no significant difference existed, probably owing to the small number of samples, the sample volumes obtained by the less-experienced pair who performed the puncture and had only 3 months of experience of EBUS-TBNA showed the same tendency as those of the more experienced pair, indicating that the cross-fanning technique is not inferior to the conventional technique, regardless of experience. However, these findings are preliminary and require further investigation in clinical practice to demonstrate that this technique leads to increased diagnostic yield and/or success rate of genetic analysis compared to the conventional technique.

Regarding the safety of this technique, it should be noted that the tip of the needle temporarily blurs on the endobronchial ultrasound (EBUS) image during the rotation maneuver. In the up-down maneuver, the EBUS image of the needle tip can be captured constantly; however, in the rotation movement, some effort is required to maintain the EBUS image of the needle tip. The presence of blood vessels inside the lymph nodes is irregular; therefore EBUS scanning should be carefully performed in advance to confirm the absence of vascular structures in the area to be punctured. The risks associated with this can be avoided by confirming the absence of blood vessels in the scanning range of the EBUS, as the movement range of the needle tip is narrower than the EBUS range. The authors believe that this technique has a better safety profile for large lesions compared to smaller ones. We also believe it is safer if the puncture is done while ensuring that the strokes are not too fast.

There are several limitations in this study. The target was silicone rubber and not human tissue; therefore, the reproducibility of these results is uncertain. Also, this is a single-center study using a small number of experiments. Though we had changed the sequences of the harvest maneuvers to ensure equal conditions for each, the sequence of the technique was not randomized. Also, operator bias may occur, as the results were different between master operators and novices. Additionally, results of the maneuvers may change depending on the location of the lymph node station or may vary depending on the stiffness or homogeneity of the lymph nodes. Further studies using biomaterials are required.

5. Conclusions

This study shows that the cross-fanning technique can increase specimen yield compared to the conventional technique but requires confirmation in future studies.

Author contributions

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Writing – original draft: Yasuyuki Mizumori.
Writing – review & editing: Yasuharu Nakahara, Tetsuji Kawamura.

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