

News Release

Title

Discovery of a simple, reliable and inexpensive method as an alternative to pathological examination to confirm the excised parathyroid gland!

A feasible way to reduce the incidence of hypoparathyroidism after thyroid surgery

Key Points

- In order to prevent hypoparathyroidism after thyroid surgery, it is necessary to perform a secure return of the excised parathyroid gland to the body. Confirmation of the excised parathyroid gland requires intraoperative pathological assessment (diagnosis by a pathologist with a microscope).
- We have developed a novel method for confirming parathyroid glands excised during surgery.
- Accuracy equivalent to rapid pathological assessment, which is a standard method, was obtained.
- Even in facilities where there is no full-time pathologist, the parathyroid gland can be confirmed easily and inexpensively.
- This method may reduce the incidence of hypoparathyroidism after thyroid surgery.

Summary

The group led by Dr. Toyone Kikumori (Associate professor of Department of Breast and Endocrine Surgery, Nagoya University Hospital) has developed a simple, reliable and inexpensive method as an alternative to pathological examinations to confirm the excised parathyroid glands.

The incidence of thyroid cancer is increasing year by year, and the number of thyroidectomy is increasing. Hypoparathyroidism is known as a postoperative complication specific to thyroid surgery. Permanent hypoparathyroidism causes very troublesome symptoms such as numbness in the limbs and tetany (muscle cramps). Inclusion of parathyroid in the excised tissue is considered the cause of hypoparathyroidism. Performing autotransplantation (transplanting into your own body) of the excised parathyroid gland is an important means of avoiding this complication.

The parathyroid gland is a very small organ. It is difficult to distinguish the parathyroid gland visually from fat and thyroid. As a standard confirmation method, intraoperative rapid pathological examinations have been performed. However, a diagnosis by a pathologist is essential.

However, the shortage of pathologists is serious all over the world, including Japan, and there are many facilities without pathologists where thyroid surgeries are performed, and autotransplantation may be performed without confirming the parathyroid gland. Insufficient

autotransplantation might be performed in such facilities.

As an alternative to rapid pathological examination during surgery, a very small part of the excised parathyroid gland-like tissue is minced and suspended in normal saline. Then, AST (GOT) and LDH in the suspension, which are biochemical test items of a general blood test are measured. It was shown that the ratio of AST to LDH can perfectly distinguish the parathyroid gland from other tissues. This method provides a means to confirm the parathyroid gland even in facilities without pathologist, which enables reliable autotransplantation, and thus the possibility of reducing the frequency of postoperative hypoparathyroidism. This method is feasible at any hospital and is inexpensive, so it can be also expected to reduce the frequency of postoperative hypoparathyroidism worldwide.

Research Background

With the development of imaging tests, the number of thyroid surgery consistently increase. On the other hand, there is a shortage of pathologists worldwide. One of the postoperative complications of thyroid surgery is hypoparathyroidism. It causes numbness in the limbs and muscle cramps (called tetany), which degrades the quality of life. Once permanent hypoparathyroidism developed, lifelong supplementation with calcium and vitamin D is essential, leading to increased medical resource consumption and economic loss. In order to prevent hypoparathyroidism, it is very important to identify the parathyroid gland that has been removed together with thyroid and to perform autotransplantation (return it into your muscles). However, the parathyroid gland may not be successfully confirmed due to a shortage of pathologists, thus, sufficient autotransplantation may not be performed, and the frequency of postoperative complications may increase.

Therefore, instead of pathological diagnosis, an alternative method to confirm the parathyroid gland during operation is necessary. If such a method is developed, it may be possible to reduce the incidence of postoperative hypoparathyroidism in situations of global pathologist shortage.

Research Results

As shown in Fig. 1, there are usually 4 parathyroid glands (arrows) on the dorsal side of the thyroid gland, but the size is a grain of rice and the color tone is very similar to fat. Even experienced surgeons sometimes have difficulty distinguishing parathyroid from fat, lymph node, thyroid, etc. (Fig. 2). During the removal of the thyroid, parathyroid gland(s) may be removed at the same time. Especially when surgery is performed for cancer, they are often removed together with the lymph nodes. Rapid pathological diagnosis is the most reliable method for confirming the removed parathyroid gland, but it is not always possible in a facility where a pathologist is not on full-time duty.

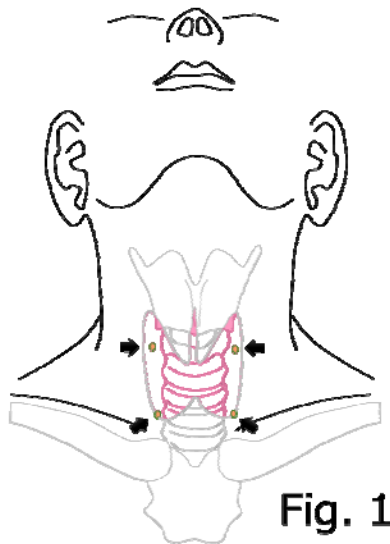


Fig. 1

Fig. 1: Position of the parathyroid glands

There are usually 4 glands on the dorsal side of the thyroid gland (arrows).

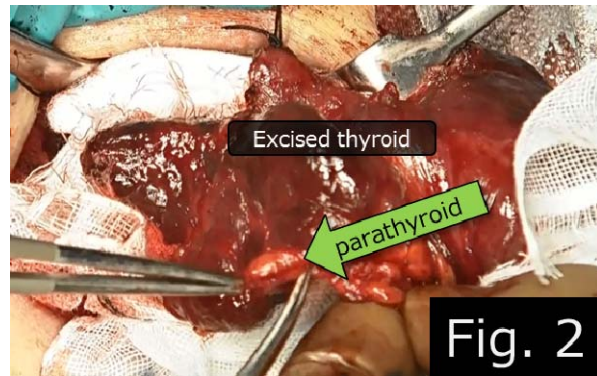


Fig. 2

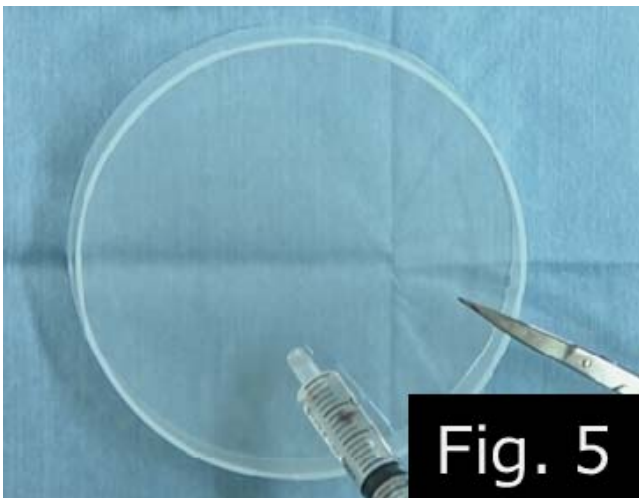
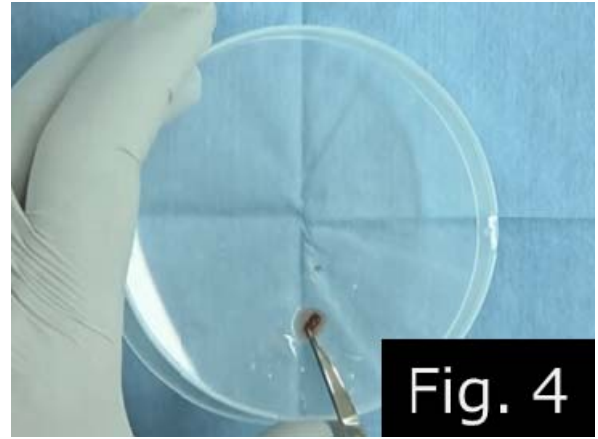
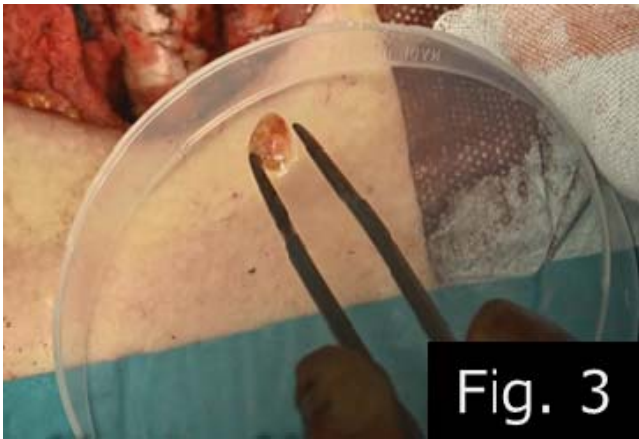
Fig. 2: Parathyroid gland adhering to the excised thyroid gland (green arrow)

Parathyroid cells are known to be very rich in mitochondria. Mitochondria utilize sugar and oxygen to produce energy, is likened to power plants of cells. An enzyme called AST (aspartate aminotransferase) plays a very important role and is abundant in mitochondria. On the other hand, LDH (lactate dehydrogenase) is an enzyme that is ubiquitous in every cell and is also involved in the production of energy in the cell. These enzymes are almost always measured in medical examinations, and can be measured very inexpensively in any hospital. Therefore, we hypothesized that the parathyroid gland could be distinguished from other tissues by calculating the ratio of AST to LDH (AST / LDH ratio).

Tissues that seemed macroscopically parathyroid gland is isolated from the excised tissue around the thyroid gland and lymphoid tissue (Fig. 3). Only a small portion (1-2 mm³) is finely minced (Fig. 4) and suspended in normal saline (Fig. 5). This operation releases AST and LDH of the tissue into the saline. The suspension is examined like normal blood samples (Fig. 6).

As shown in the graph (Fig. 7), the AST / LDH ratio of the parathyroid gland is clearly higher than that of other tissues, the threshold value to 0.27 can completely differentiate parathyroid from other tissues.

This result made it possible to easily and inexpensively confirm the excised parathyroid gland during the operation. Comparable accuracy to pathological diagnosis leads to the reliable confirmation of parathyroid and sufficient autotransplantation even in a facility without pathologists. It is expected to reduce the incidence of postoperative hypoparathyroidism.



Sample processing procedure

Fig. 3: Parathyroid gland-like tissue isolated from excised tissue

Fig. 4: Mince a 1-2mm cubic tissue excised from the isolated tissue

Fig. 5: Suspend in 1-1.5 mL of normal saline

Fig. 6: Submit to a biochemical test similar to a blood sample

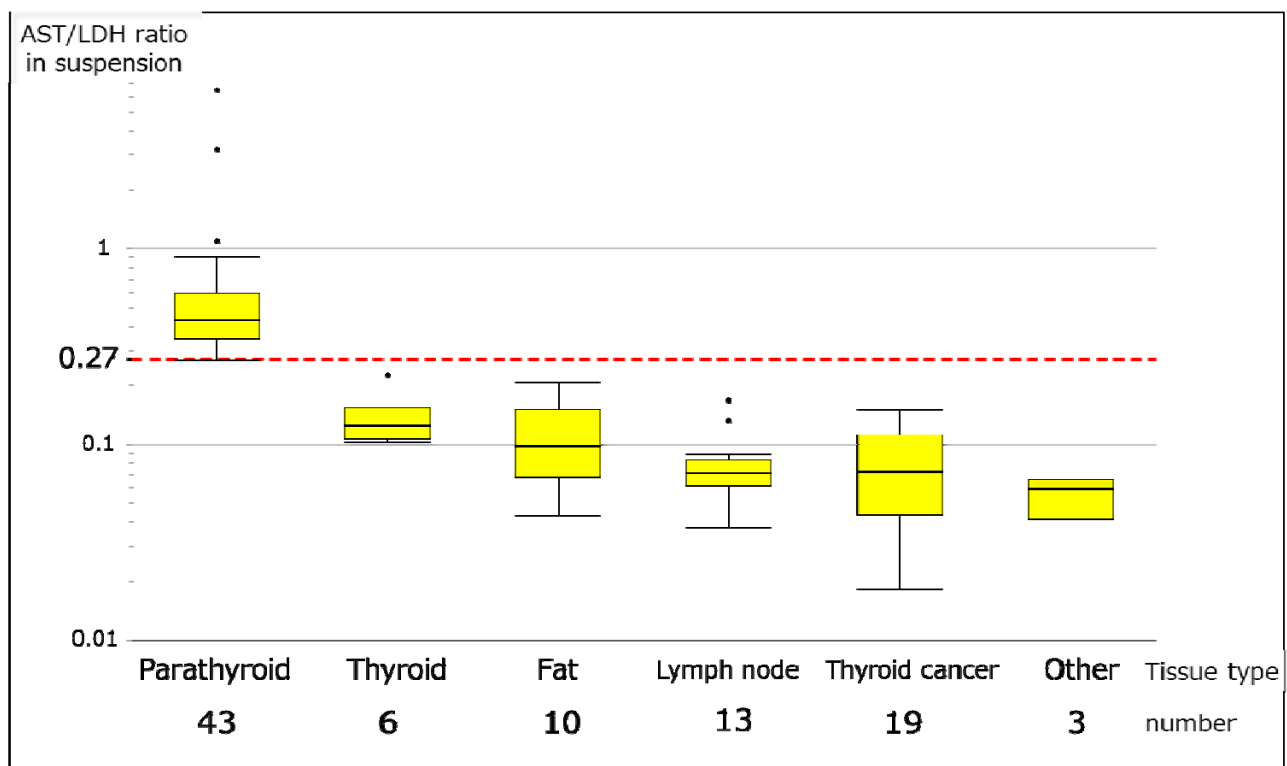


Fig. 7

Fig. 7: Graph showing AST/LDH ratio in each tissue suspension logarithmically. Yellow rectangles indicate the range from the upper quarter to the third quarter. The bold horizontal bars in the rectangle indicate the median value. The horizontal bars above and below the rectangle indicate the maximum and minimum values. Black points indicate outliers based on statistical judgment. The red dotted line indicates the threshold (0.27) that distinguishes the parathyroid gland from other tissues.

Research Summary and Future Perspective

This study shows that parathyroid glands can be confirmed very inexpensively, easily, and most importantly without pathological diagnosis. We plan to conduct a validation test to verify whether the current results can be reproduced with a POCT (Point Of Care Testing) device that can be installed in the operating room for actual clinical application.

Also, there is a shortage of pathologists worldwide, especially in developing countries. Thyroid surgery is increasing with the development of imaging tests. However, reliable confirmation of parathyroid may not be performed due to a shortage of pathologists, and the frequency of postoperative complications may increase. By spreading the results of this research worldwide, a reduction of the incidence of postoperative hypoparathyroidism can be expected.

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