Author's response to reviews

**Title:** Total parathyroidectomy with trace amounts of parathyroid tissue autotransplantation as the treatment of choice for secondary hyperparathyroidism: A Single-Center Experience

**Authors:**

Qingqing He (heqingqing@yeah.net)
Dayong Zhuang (zdyddv2000@tom.com)
Luming Zheng (oliverzhenglu3@126.com)
Ziyi Fan (miastelo@tom.com)
Peng Zhou (weardzp@126.com)
Jian Zhu (zhuijiansdu@126.com)
Songjian Duan (duansongjian123@163.com)
Yanning Li (liyanningn@126.com)
Yanming Ge (jjzyygym@126.com)
Zhen Lv (tengzhoulyzen@163.com)
Lei Cao (caolei0841020027@163.com)

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**Author's response to reviews:** see over
1. Q  Transcervical thymectomy is part of the 3 standard procedures, at least you have to mention it in the discussion (p12).

   A  Yes, transcervical thymectomy is an important step of total total parathyroidectomy. And it shows in my added part in Discussion.

2. Q  Graft dependent hyperparathyroidism is not (!) extremely rare, it is 9.3% in the tominaga paper and we have similar data after more than 350 operations.

   A  I agree with you about that graft dependent hyperparathyroidism is not rare according to the current literature reports. But according to our follow-up result, there is no graft dependent recurrence observed. Minor amount of parathyroid graft (30mg) was applied in our study, comparing to 100mg or more amount of transplanted tissue in other reports. The difference in graft quantity applied maybe one of reasons of recurrence discrepancy. In our opinion, low recurrent rate may be caused by transplanting minor parathyroid, but limited number of cases and short follow-up may also possible reasons. Further studys are needed to verify our result.

3. Q  According to your manuscript you have no experience with removal of autografts. So how can you say that it is simple. Sometimes it can be necessary to remove a great part of the scm-muscle.

   A  Ipsilateral sterno-cleido-mastoid muscle cross to skin incision is adopted as graft site in our study, and nonabsorbable suture material is used to close the SCM muscle as a mark of graft site if removal of autografts is necessary. Actually in the beginning we used a silver clip in the graft site as marker, but a shift of implanted silver clip was observed by ultrasound. So silver clip was not used. The reason why forearm muscle is not adopted in our study is that our
patients mostly are advanced staged and artificial arteriovenous fistula is common in both forearms. For these patients, forearm muscle is not appropriate to be treated as graft site anymore. So we choose SCM muscle as graft site and transplant operation on nearby muscle was much simpler and more convenient without another incision. And if graft dependent recurrent occurred, graft tissue and some part of SCM muscle would be removed under local anesthesia.

Recurrent HPT after total parathyroidectomy with autotransplantation is usually due to the overgrowth of the autograft. We consider thirty pieces of 1 x 1 x 3 mm parathyroid tissue (about 100 micrograms) too much. Ten pieces of 1 x 1 x 3 mm parathyroid tissue (about 30 micrograms) would be enough. For patients who demand long-term hemodialysis after parathyroidectomy, the risk of recurrence is not negligible. Thus, to avoid recurrent HPT, all parathyroids, including supernumerary glands, should be identified. In our series, 35.1% of the inferior glands were located in thymic tongue. If the surgeon cannot identify 4 glands, removal of thymic tissue from the neck incision is essential to avoid missing glands. Most patients underwent artificial arteriovenous fistula in bilateral forearms for hemodialysis. We believe it would be easier and safer to remove residual parathyroid tissue from sternocleidomastoid muscle at recurrence as compared to from the forearm. Reoperation may be relatively simple for recurrent hyperparathyroidism induced by the hyperfunction of autografted parathyroid tissue, because surgical access to
sternocleidomastoid muscle is simple, and it does not require general anesthesia, also avoid the risk of major surgical complications such as laryngeal nerve injury.

4. Q Tc-MIBI-SPECT/CT can hardly distinguish between graft dependent recurrence in the scm-muscle and a hyperplastic parathyroid remnant on the same side

   A Yes, Tc-MIBI-SPECT can hardly distinguish between graft dependent recurrence in the scm-muscle and a hyperplastic parathyroid remnant on the same side. But SPECT-CT (99m)Tc-MIBI imaging combined CT scan could show the precise localization and discrimination of whether it is a graft dependent recurrence in the scm-muscle or a hyperplastic parathyroid remnant on the same side. SPECT-CT (99m)Tc-MIBI imaging combined CT scan technique possesses the advantage of both anatomic and metabolic imaging, and its application in localization of recurrent site is more precise than Tc-MIBI-SPECT.

The pictures below are about one hyperparathyroidism patient from the department of nuclear medicine of our hospital.

Preoperative CT-MIBI image fusion is a new imaging modality that enabled reliable and precise localization of the parathyroid. This technique consists of taking MIBI-SPECT and CT separately, using a fixation unit that provides reproducible positioning of the patients’ neck.
Image fusion of SPECT-CT ~(99m) Tc-MIBI imaging combined CT

Image of Tc-MIBI-SPECT
5.Q As I told before, 25-Hydroxyvitamin D3 has is not relevant in secondary hyperparathyroidism.

A Yes, 25-Hydroxyvitamin D3 is not relevant in secondary hyperparathyroidism. Now laboratory examination of 1,25-Hydroxyvitamin D3 is not available in most Chinese hospitals. So in the future if examination of 1,25-Hydroxyvitamin D3 be possible, it will be applied in our work.