



Transoral Endoscopic Thyroidectomy Vestibular Approach: Lessons from a Five Years' Experience

11

Daqi Zhang, Gianlorenzo Dionigi, Francesco Frattini,
Andrea Cestari, Antonella Pino, Ozer Makay, Che-Wei Wu,
Hoon Yub Kim, Andrea Casaril, and Hui Sun

11.1 Introduction

Surgery on the thyroid gland is one of the most common procedures in head and neck surgery. Open thyroid surgery is considered safe, with a rate of 0.8–2.3% permanent recurrent nerve palsy, 9–10% permanent hypoparathyroidism, and < 1% mortality for benign nodular goiter [1]. The thyroid gland is traditionally accessed via the classic cross-section according to Theodor Kocher.

The neck is a highly visible part of the body and the desire for scarless thyroid surgery is increasing, especially among patients in Asian countries. Since the first clinical series on endoscopic parathyroid surgery published by Gagner in 1996 [2],

D. Zhang

Division of Thyroid Surgery, China-Japan Union Hospital of Jilin University,
Changchun, Jilin, China
e-mail: daqizhang@yeah.net

G. Dionigi

Division of General Surgery, IRCCS Istituto Auxologico Italiano, Milan, Italy
Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
e-mail: gianlorenzo.dionigi@unimi.it

F. Frattini (✉) · A. Cestari · A. Pino

Division of General Surgery, IRCCS Istituto Auxologico Italiano, Milan, Italy
e-mail: f.frattini@auxologico.it; a.cestari@auxologico.it; pino.antonella@virgilio.it

O. Makay

Department of General Surgery, Division of Endocrine Surgery, Ege University Hospital,
Izmir, Turkey
e-mail: ozermakay@ege.edu.tr

C.-W. Wu

Department of Otolaryngology-Head and Neck Surgery, Kaohsiung Medical University
Hospital, Kaohsiung, Taiwan
e-mail: cwwu@kmu.edu.tw

© The Author(s) 2024

M. Testini, A. Gurrado (eds.), *Thyroid Surgery*, Updates in Surgery,
https://doi.org/10.1007/978-3-031-31146-8_11

101

H. Y. Kim

Korea University College of Medicine Thyroid Center, Department of Surgery,
Korea University Hospital, Seoul, South Korea
e-mail: hoonyubkim@korea.ac.kr

A. Casaril

Endocrine Surgery Unit, Pederzoli Hospital, Verona, Italy
e-mail: andrea.casaril@ospedalepederzoli.it

H. Sun (✉)

Laboratory of Molecular Biology and Translational Medicine on Differentiated Thyroid
Carcinoma, Changchun, Jilin, China
e-mail: s_h@jlu.edu.cn

many different minimally invasive or endoscopic procedures of thyroid and parathyroid surgery have been described in the last twenty years. Minimally invasive surgery of the neck, which encompasses minimally invasive video-assisted thyroidectomy [3], bilateral axillary approach [4, 5] and other approaches [6], is not very popular due to its complexity and longer learning curve. Additionally, it often results in external scars.

With the goal of achieving a scar-free anterior neck and using direct transoral laparoscopy, Anuwong developed the transoral endoscopic thyroidectomy vestibular approach (TOETVA) and published the first large clinical series with 60 patients [7]. Due to its simplicity, his method is gaining acceptance in thyroid and parathyroid surgery [8–12].

In this chapter, we describe our clinical experience and discuss some technical issues regarding this new procedure.

11.2 Patients and Methods

The series was conducted from 2017 to 2021. Prior approval was obtained from the local ethics committee. Of 210 eligible patients, 100 (47%) opted for endoscopic access. Surgery was performed under general anesthesia with orotracheal intubation. Patients were placed in the supine position with the head slightly tilted. The surgeon stood directly behind the patient's head, and the camera assistant was to the right of the surgeon. The laparoscopic tower was high-resolution and contributed to a magnified and optimized image. First, a 10-mm transverse incision was made in the middle of the oral vestibule, followed by injection of epinephrine and saline through a Veress cannula [1] with hydrodissection of the entire surgical field under the platysma muscle (Figs. 11.1, 11.2, and 11.3). Then, the blunt dissector rod was inserted and carefully moved in different directions and from left to right, manually sparing the external jugularis to create a space between the platysma, jugularis, and infrahyoid muscle. A 12-mm trocar could then be inserted, followed by a 30-degree telescope. The gas pressure was set at 6 mmHg. Two additional 5-mm trocars were introduced to the right and left of the middle trocar. The lateral trocars must be placed cranially and well lateral to the canines on the inside of the lower lip to avoid injury to the mental nerve. The working space was then prepared below the

Fig. 11.1 Vestibular incisions and trocar insertion

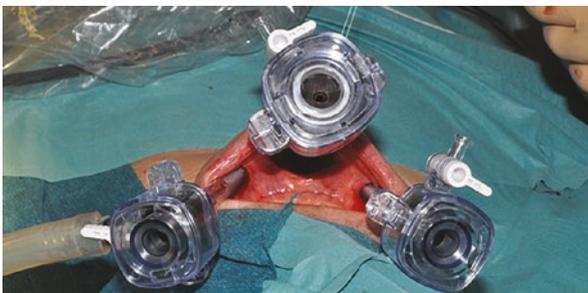


Fig. 11.2 Veress needle insertion



Fig. 11.3 Trocar insertion

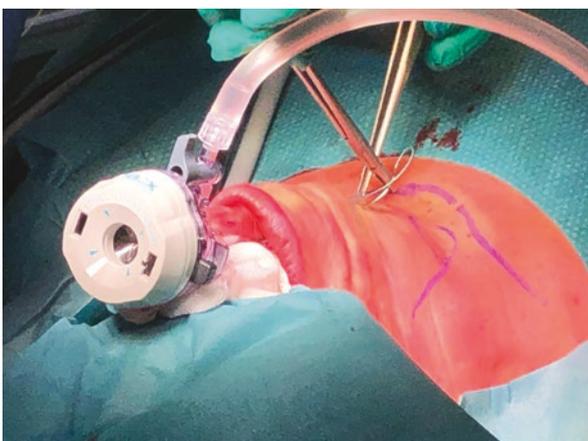
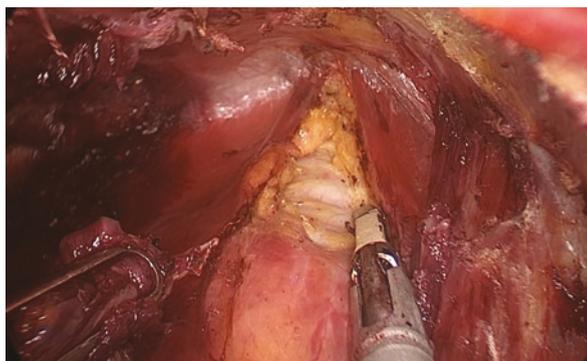


Fig. 11.4 Outward retraction of cervical recti muscles



Fig. 11.5 Intraoperative view



platysma. This was bounded cranially by the larynx, caudally by the jugulum, and laterally by the sternocleidomastoid muscles. Dissection of the thyroid gland began with dissection of the linea alba cervicalis. For better exposure, the cervical recti muscles were retracted laterally by the second assistant with a suture passed outward (Figs. 11.4 and 11.5). The isthmus of the thyroid gland was transected. Ultracision (Ethicon Endosurgery, Cincinnati, OH, USA) was used for dissection and closure of the vessels. Immediately after transection of the isthmus, the recurrent laryngeal nerve (RLN) was exposed. Dissection of the RLN was performed without electrocautery or ultrasonic scissors to avoid thermal damage. After transection of the superior polar vessels, dissection was performed from cranial to caudal, and the RLN could be visualized and followed retrogradely from its immersion in the larynx. Intraoperative neuromonitoring (IONM) was routinely performed with the C2 NerveMonitor (Inomed Medizintechnik GmbH, Emmendingen, Germany), either through a trocar or directly percutaneously through a 1-mm skin incision. In this way, the location and function of the RLN and superior laryngeal nerve could be verified. The specimen was retrieved through the midline 12-mm incision in a collection bag (Eco-Sac, Espiner medical, Measham, UK). The

Fig. 11.6 Postoperative wound on the inside of the lower lip



infrahyoid musculature was adapted medially with VLOC 3–0 absorbable running suture (Covidien, Mainsfield, MA, USA). The oral incisions were closed with absorbable suture (Vicryl 5–0, Ethicon, Livingstone, UK). A pressure dressing was applied to compress the chin overnight. Perioperative antibiotic prophylaxis (sulbactam-ampicillin, UNACID) was administered i.v. 30 minutes before skin incision and then administered p.o. for a total of 5 days. In addition, patients performed a disinfecting mouth rinse after each meal for a total of 5 days (Fig. 11.6).

11.3 Results

One hundred patients underwent TOETVA, including 87 women and 13 men. The patients' neck morphology was not a criterion for selection or exclusion. Operative time was longer in patients with wide necks than in those with slender necks. Overweight or obesity was not a contraindication. Fifteen patients had a body mass index (BMI) between 25 and 30 kg/m² and five patients had a BMI >30 kg/m². In this first case series, optimal access and visualization of the cervical anatomy was possible. All important anatomical structures (such as the parathyroid glands, the superior thyroid artery, the inferior thyroid artery, the RLN) could be imaged with excellent resolution and easily identified in overview. The parathyroid glands were identified and preserved. Nodule diameter measured on preoperative ultrasound ranged from 0.3 to 6.5 cm (mean 3.1 ± 1.8) with a mean volume ranging from 2.5 to 159 mm³ (mean 24 ± 41.2 mm³). All patients had a nodule smaller than 7 cm. The procedures performed were 80 lobo-isthmectomies, and 20 total thyroidectomies. The average weight of surgical specimens was 21.9 ± 12.2 (10–110) g. The specimen was harvested through the 12-mm incision. Surgical times averaged 184 minutes. Five cases (5%) required conversion to an open cervical incision. Conversion was required due to hemorrhage.

No postoperative complications occurred, and the mean postoperative stay was 3 days. Transient leukocytosis was noted on postoperative day 1 and normalized by postoperative day 3. All patients resumed oral feeding in the evening of the

procedure. Cosmetic results were excellent, with no visible scars. During the first 3 postoperative days, the maximum pain intensity did not exceed 3 points on the visual analog pain scale in any case. Histologically, there were 15 papillary carcinomas (all were discovered at final pathology). All of these lesions were < 15 mm in size. There were 6 benign oncocytic nodules, 9 thyrotoxic nodules, and 70 benign nodules or goiters that were symptomatic. In six cases, a parathyroid gland was identified intraoperatively on the surgical specimen and systematically reimplanted into the sternocleidomastoid muscle. The pathologist found six parathyroid glands in the surgical specimens of six patients. There were no postoperative hematomas. However, ten patients (10%) experienced postoperative bruising or ecchymosis, which was transient and resolved within 10 days. Two patients developed a cervical seroma, which was treated with needle aspiration. There were no cases of surgical site infection. Five of 20 patients who underwent total thyroidectomy developed transient hypoparathyroidism (25%). No cases of permanent hypoparathyroidism. Six patients (6%) developed temporary paralysis of the RLN. Functional recovery was evidenced by normal vocal cord mobility seen by transnasal endoscopy between 1 and 4 months. There were no cases of permanent paralysis of the RLN. Sublabial and chin hypoesthesias or paresthesias were observed in the first 25 patients and lasted 3–12 weeks. Therefore, in subsequent patients, we preferred to avoid thermal coagulation and performed blunt dissection with Kelly forceps. Thereafter, we observed no further cases of postoperative dysesthesia lasting longer than 4 weeks. One patient had a cervical skin burn that occurred during creation of the workspace, which resolved with topical corticosteroids and showed a good cosmetic result after 2 months. One patient reported persistent sublabial paresthesias over an area of 1 cm² at the 3-month follow-up. Finally, on the first day after surgery one patient reported chest pain, after which a CT scan was performed revealing pneumomediastinum; this resolved spontaneously.

11.4 Discussion

Despite continuous progress for more than 20 years, the acceptance of the minimally invasive approach in thyroid surgery is still very low, partly due to the difficult learning curve of the proposed methods and possibly due to the remaining scars. The transoral approach has proven to be ideal because it leaves no cutaneous scars. It also provides anatomic and layered access to the surgical site on both sides of the trachea without muscle transection, thus minimizing surgical trauma. On the other hand, the transoral approach to the neck means that sterile surgery can lead to a potentially contaminated procedure with the disadvantage of deep wound infection.

Witzel et al. developed the concept of transoral thyroid surgery in studies of cadavers and animal models, initially using a sublingual approach [13]. Benhidjeb et al. and Wilhelm et al. described many potential problems with the peroral approach via the floor of the mouth [14, 15]. These include a higher conversion rate, postoperative swelling and dysphagia, which may affect patient safety.

Other investigators pursued the peroral approach. Nakajo et al. described their TOVANS (trans-oral video-assisted neck surgery) method as a gasless transoral endoscopic thyroidectomy with a single large incision as the premandibular approach and anterior neck skin lift [16]. They performed eight procedures. All patients had sensory disturbances of the chin that lasted more than 6 months after surgery. RLN palsy occurred in one patient, and no mental nerve palsy or infection was detected.

Yang et al. performed a study of 82 patients who underwent either endoscopic thyroidectomy via the oral vestibular approach (ETOVA) or endoscopic thyroidectomy via the areolar approach (ETAA) [8]. They showed no statistical differences in operative time, complications or patient satisfaction, but the transoral technique showed better cosmetic results.

Anuwong in Thailand refined the technique called TOETVA and reported excellent results in an initial study of 60 patients [7]. The results were as safe as conventional open thyroid surgery. In his last series of 425 cases, there were no cases of infection or permanent nerve palsy, 5.9% of patients had temporary vocal cord palsy, and 10.9% had temporary hypoparathyroidism [17]. In their landmark study in Europe, Dionigi et al. in Milan, Italy, reported their first experience with TOETVA performed in 15 cases, with a low complication rate [10]. As in our study and in contrast to Anuwong's series, the group used orotracheal rather than nasotracheal intubation, which simplified the intubation technique and IONM. The importance of IONM has been highlighted in many studies of open and minimally invasive thyroidectomy [18–24] and is recognized by our group. In our experience vagus nerve stimulation has been done in transoral endoscopic thyroidectomy as in the open procedure. The stimulation has been omitted in unilateral procedures only, but it must be performed in bilateral procedures [25, 26].

Our initial clinical experience showed longer operative times but with an excellent safety profile, with clear identification of critical anatomy and the use of IONM [27, 28]. The patients' postoperative pain scores were low and the cosmetic outcomes were excellent. Skin necrosis, major hematoma, sensory disturbances or end-oral damage did not occur in any of the patients in our case series. The technique could be performed with standard laparoscopic instruments, with minor modifications in initial dissection, insufflation, and team positioning. Although there is no reliable evidence for the use of perioperative antibiotics in transoral procedures [29], the authors still opted for perioperative antibiotic prophylaxis. This can certainly be significantly shortened or even omitted. The published series by Anuwong et al. did not show high infection rates [17]. The authors consider preoperative disinfecting mouth rinses to be as important as antibiotic prophylaxis, although the evidence is equally lacking. The following technical aspects have been identified:

- The team's position and technical advancement with the 4 K endoscopic tower is of great importance for better visualization of the anatomy [30–33].
- The lateral and far cranial positioning (approx. 1 cm caudal to the vermilion of the lips on the inside and opposite the canines) of the 5-mm trocars is intended to avoid damage to the mental nerve [34–37].
- The subplatysmal hydrodissection with adrenaline solution allows creation of a non-existent space [38–40].

- Use of the bougie rod/dilator through the 12-mm incision increases the surgical space in the anterior neck [41–43].
- Stubborn tissue bridges are resolved by monopolar or ultrasonic dissection. It is important to expose the subplatysmal area up to the jugular fossa [44].
- The infrahyoid muscles are temporarily retracted laterally using percutaneous sutures. Midline, support sutures are stitched subcutaneously to enlarge the surgical site by traction upwards [45].
- Routine IONM serves to assess the localization and function of the RLN. This can be done through the trocars or percutaneously through a 1-mm incision [46].
- The specimen is extracted in a recovery bag. In the case of large specimens, dissection of the thyroid within the pouch may be necessary, but this should be avoided at all costs in favor of histological evaluation [46].
- Drainage can usually be avoided [46].
- Perioperative and postoperative antibiotics and disinfecting mouth rinses are continued for 5 days postoperatively as infection prophylaxis [46].

Funding This work was supported by the Eurocrine Project (Auxologico IRCCS).

References

1. Rayes N, Seehofer D, Neuhaus P. The surgical treatment of bilateral benign nodular goiter. Balancing invasiveness with complications. *Dtsch Arztebl Int.* 2014;111(10):171–8.
2. Gagner M. Endoscopic subtotal parathyroidectomy in patients with primary hyperparathyroidism. *Br J Surg.* 1996;83(6):875.
3. Miccoli P, Materazzi G. Minimally invasive, video-assisted thyroidectomy (MIVAT). *Surg Clin North Am.* 2004;84(3):735–41.
4. Shimazu K, Shiba E, Tamaki Y, et al. Endoscopic thyroid surgery through the axillo-bilateral-breast approach. *Surg Laparosc Endosc Percutan Tech.* 2003;13(3):196–201.
5. Strik MW, Anders S, Barth M, et al. Total-videoendoskopische Strumaresektion via “axillo-bilateral breast approach”. *Operative Technik und erste Ergebnisse [Total videoendoscopic thyroid resection by the axillo-bilateral breast approach. Operative method and first results]. Chirurg.* 2007;78(12):1139–44.
6. Phillips HN, Fiorelli RK, Queiroz MR, et al. Single-port unilateral transaxillary totally endoscopic thyroidectomy: a survival animal and cadaver feasibility study. *J Minim Access Surg.* 2016;12(1):63–7.
7. Anuwong A. Transoral endoscopic thyroidectomy vestibular approach: a series of the first 60 human cases. *World J Surg.* 2016;40(3):491–7.
8. Yang J, Wang C, Li J, et al. Complete endoscopic thyroidectomy via oral vestibular approach versus areola approach for treatment of thyroid diseases. *J Laparoendosc Adv Surg Tech A.* 2015;25(6):470–6.
9. Pai VM, Muthukumar P, Prathap A, et al. Transoral endoscopic thyroidectomy: a case report. *Int J Surg Case Rep.* 2015;12:99–101.
10. Dionigi G, Bacuzzi A, Lavazza M, et al. Transoral endoscopic thyroidectomy: preliminary experience in Italy. *Updat Surg.* 2017;69(2):225–34.
11. Wang C, Zhai H, Liu W, et al. Thyroidectomy: a novel endoscopic oral vestibular approach. *Surgery.* 2014;155(1):33–8.
12. Udelsman R, Anuwong A, Oprea AD, et al. Trans-oral vestibular endocrine surgery: a new technique in the United States. *Ann Surg.* 2016;264(6):e13–6.

13. Witzel K, von Rahden BH, Kaminski C, Stein HJ. Transoral access for endoscopic thyroid resection. *Surg Endosc.* 2008;22(8):1871–5.
14. Benhidjeb T, Wilhelm T, Harlaar J, et al. Natural orifice surgery on thyroid gland: totally transoral videoassisted thyroidectomy (TOVAT): report of first experimental results of a new surgical method. *Surg Endosc.* 2009;23(5):1119–20.
15. Wilhelm T, Metzigg A. Video. Endoscopic minimally invasive thyroidectomy: first clinical experience. *Surg Endosc.* 2010;24(7):1757–8.
16. Nakajo A, Arima H, Hirata M, et al. Trans-oral video-assisted neck surgery (TOVANS). A new transoral technique of endoscopic thyroidectomy with gasless premandible approach. *Surg Endosc.* 2013;27(4):1105–10.
17. Anuwong A, Ketwong K, Jitpratoom P, et al. Safety and outcomes of the transoral endoscopic thyroidectomy vestibular approach. *JAMA Surg.* 2018;153(1):21–7.
18. Dralle H, Sekulla C, Haerting J, et al. Risk factors of paralysis and functional outcome after recurrent laryngeal nerve monitoring in thyroid surgery. *Surgery.* 2004;136(6):1310–22.
19. Wang Y, Yu X, Wang P, et al. Implementation of intraoperative neuromonitoring for transoral endoscopic thyroid surgery: a preliminary report. *J Laparoendosc Adv Surg Tech A.* 2016;26(12):965–71.
20. Patel PN, Jayawardena ADL, Walden RL, et al. Evidence-based use of perioperative antibiotics in otolaryngology. *Otolaryngol Head Neck Surg.* 2018;158(5):783–800.
21. Oliva A, Grassi S, Zedda M, et al. Ethical and medico-legal issues of TOETVA procedure and simulation on cadavers: a scoping review. *Eur Rev Med Pharmacol Sci.* 2022;26(13):4550–6.
22. Celik S, Bilge O, Ozdemir M, et al. Modified Larssen solution (MLS)-fixed cadaver model for transoral endoscopic thyroidectomy vestibular approach (TOETVA) education: a feasibility study. *Surg Endosc.* 2022;36(7):5518–30.
23. Bertelli AAT, Lira RB, Gonçalves AJ, et al. Transoral endoscopic thyroidectomy vestibular approach (TOETVA): pioneers’s point of view. *Arch Endocrinol Metab.* 2021;65(6):858–9.
24. Zhang D, Wu CW, Wang T, et al. Drawbacks of neural monitoring troubleshooting algorithms in transoral endoscopic thyroidectomy. *Langenbeck's Arch Surg.* 2021;406(7):2433–40.
25. Cohen O, Tufano RP, Anuwong A, et al. Trans-oral endoscopic thyroidectomy vestibular approach (TOETVA) for the pediatric population: a multicenter, large case series. *Surg Endosc.* 2022;36(4):2507–13.
26. Zhang D, Fu Y, Zhou L, et al. Pictorial essay of vestibular incision outcomes from transoral endoscopic thyroidectomy. *Langenbeck's Arch Surg.* 2021;406(8):2869–77.
27. Zhang D, Sun H, Tufano R, et al. Recurrent laryngeal nerve management in transoral endoscopic thyroidectomy. *Oral Oncol.* 2020;108:104755.
28. Zhang D, Wang T, Kim HY, et al. Strategies for superior thyroid pole dissection in transoral thyroidectomy: a video operative guide. *Surg Endosc.* 2020;34(8):3711–21.
29. Erol V, Dionigi G, Barczyński M, et al. Intraoperative neuromonitoring of the RLNs during TOETVA procedures. *Gland Surg.* 2020;9(Suppl 2):S129–35.
30. Zhang D, Famá F, Caruso E, et al. How to avoid and manage mental nerve injury in transoral thyroidectomy. *Surg Technol Int.* 2019;35:101–6.
31. Zhang D, Fu Y, Dionigi G, et al. Human cadaveric model for studying the preservation of mental nerve during transoral endoscopic thyroidectomy. *Surg Radiol Anat.* 2020;42(1):55–62.
32. Zhang D, Li S, Dionigi G, et al. Animal study to evaluate the effect of carbon dioxide insufflation on recurrent laryngeal nerve function in transoral endoscopic thyroidectomy. *Sci Rep.* 2019;9(1):9365.
33. Zhang D, Li S, Dionigi G, et al. Stimulating and dissecting instrument for transoral endoscopic thyroidectomy: proof of concept investigation. *Surg Endosc.* 2020;34(2):996–1005.
34. Zhang D, Park D, Sun H, et al. Indications, benefits and risks of transoral thyroidectomy. *Best Pract Res Clin Endocrinol Metab.* 2019;33(4):101280.
35. Zhang D, Caruso E, Sun H, et al. Classifying pain in transoral endoscopic thyroidectomy. *J Endocrinol Investig.* 2019;42(11):1345–51.
36. Celik S, Makay O, Yoruk MD, et al. A surgical and anatomic-histological study on transoral endoscopic thyroidectomy vestibular approach (TOETVA). *Surg Endosc.* 2020;34(3):1088–102.

37. Zhang D, Wu CW, Inversini D, et al. Lessons learned from a faulty transoral endoscopic thyroidectomy vestibular approach. *Surg Laparosc Endosc Percutan Tech.* 2018;28(5):e94–9.
38. Russell JO, Anuwong A, Dionigi G, et al. Transoral thyroid and parathyroid surgery vestibular approach: a framework for assessment and safe exploration. *Thyroid.* 2018;28(7):825–9.
39. Zhang D, Li S, Dionigi G, et al. Feasibility of continuous intraoperative neural monitoring during transoral endoscopic thyroidectomy vestibular approach in a porcine model. *J Laparoendosc Adv Surg Tech A.* 2019;29(12):1592–7.
40. Dionigi G, Wu CW, Tufano RP, et al. Monitored transoral endoscopic thyroidectomy via long monopolar stimulation probe. *J Vis Surg.* 2018;4:24.
41. Dionigi G, Chai YJ, Tufano RP, et al. Transoral endoscopic thyroidectomy via a vestibular approach: why and how? *Endocrine.* 2018;59(2):275–9.
42. Anuwong A, Sasanakietkul T, Jitpratoom P, et al. Transoral endoscopic thyroidectomy vestibular approach (TOETVA): indications, techniques and results. *Surg Endosc.* 2018;32(1):456–65.
43. Anuwong A, Kim HY, Dionigi G. Transoral endoscopic thyroidectomy using vestibular approach: updates and evidences. *Gland Surg.* 2017;6(3):277–84.
44. Russell JO, Clark J, Noureldine SI, Anuwong A. Transoral thyroidectomy and parathyroidectomy – a north American series of robotic and endoscopic transoral approaches to the central neck. *Oral Oncol.* 2017;71:75–80.
45. Dionigi G, Lavazza M, Bacuzzi A, et al. Transoral endoscopic thyroidectomy vestibular approach (TOETVA): from a to Z. *Surg Technol Int.* 2017;30:103–12.
46. Dionigi G, Bacuzzi A, Lavazza M, et al. Transoral endoscopic thyroidectomy via vestibular approach: operative steps and video. *Gland Surg.* 2016;5(6):625–7.

Open Access This chapter is licensed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits any noncommercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if you modified the licensed material. You do not have permission under this license to share adapted material derived from this chapter or parts of it.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

