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HEAD AND NECK

Effect of near infrared autofluorescence guided total thyroidectomy on postoperative hypoparathyroidism: a randomized clinical trial

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Abstract

Purpose The purpose of this single-blinded, 2-centre, randomized controlled trial was to test if near-infrared (NIR) autofluorescence image guidance for parathyroid gland (PG) detection during total thyroidectomy can reduce the incidence of hypoparathyroidism in both malignant and benign cases.

Method Patients admitted for primary or completion total thyroidectomy were randomized to either the NIR intervention group or the standard care NONIR (no near infrared) group. The primary endpoint was the rate of hypoparathyroidism at the 3-month follow-up, defined as hypocalcemia and inappropriately low parathyroid hormone levels and/or continuous treatment with active vitamin D. The secondary endpoint was the PG identification rate.

Results A total of 147 patients were included of whom 73 were allocated to NIR. Primary or completion thyroidectomy was conducted in 84 and 63 cases, respectively. A total of 130 completed 3 months follow-up. Postoperative hypoparathyroidism in the NIR group at 12 h, 1 month and 3 months was, respectively, 31.8, 14.1, 6.5% compared with 35.9, 18.9, 11.8% in the NONIR group (all $p > 0.46$). In the NIR group, the identification rate of PGs was 69.5% (146 of 210 PGs), and 9% (19 of 210 PGs) were identified only due to additional use of NIR. For 15 out of 69 patients (21.7%) additionally PGs was found.

Conclusion Hypoparathyroidism was nominally less frequent in the NIR group, although not statistically significant. Further studies are needed to confirm if NIR may be a supportive PG identification tool to minimize the number of PG which would have been otherwise missed, especially during more complicated thyroid procedures.

Trial registry ClinicalTrials.gov: NCT04193332. Registration date: 16.08.2019.

Keywords Near-infrared autofluorescence · Parathyroid glands · Hypoparathyroidism · Hypocalcemia · Thyroidectomy

Background

Hypoparathyroidism (HypoPT) is the most frequent complication to thyroid surgery [1–5]. A recent review reported a median postoperative incidence of 27.5% for transient and 2.2% for permanent hypocalcemia and point out a significant variation in the literature also with regards to the definition of permanent HypoPT [5]. Other authors state that permanent HypoPT is underestimated [4] reporting incidences up to 17.4% [1, 6–8]. This variation is most likely due to lack of agreement on how to define both HypoPT and transient/permanent HypoPT, which makes study comparison difficult [4, 9, 10].

Due to their small size and resemblance to thyroid tissue, lymph nodes or brown fat, intraoperative identification of the parathyroid glands (PGs) can be challenging. Significant risk of damage or accidental excision of the PGs exist, even when minimizing intraoperative manipulation [11].

Our definition of HypoPT is based on *European Society of Endocrinology Clinical Guideline* [3] in which HypoPT is characterized by hypocalcemia (ion-$Ca^{2+} < 1.15$ mmol/L.) and inappropriately low parathyroid hormone levels and/or continuous treatment with active vitamin D. This condition is considered permanent if lasting for 6 months or more and/or if continuous treatment with calcium and active vitamin D is needed [3]. Permanent HypoPT is associated with increased

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mortality, morbidity, impaired quality of life and long-term complications, particularly renal, neuropsychiatric and musculoskeletal comorbidities due to generalized calcification [12–17].

Intraoperative autofluorescence-based identification of the PGs using near-infrared (NIR) light is an emerging technique and several feasibility studies have demonstrated its effectiveness for PG identification [18–27]. Without this technique the identification of PGs relies on frozen section or the surgeon's level of experience.

When PGs are exposed to NIR excitation light with a wavelength of 805 nm, the intrinsic fluorophore emits light in the near-infrared spectrum (700–900 nm). The emitted light can be detected by a camera, which produces real-time imaging to allow surgical guidance. The fluorescent molecule specific for the PG has not yet been identified [18, 28, 29].

The aim of this randomized clinical trial was to examine the potential of NIR imaging-guided PG detection in thyroid surgery and the possible reduction in postoperative HypoPT.

Methods

This prospective randomized controlled trial (RCT) was approved by The Danish National Committee on Health Research Ethics and was conducted between August 2019 and May 2021. Patients admitted for primary total thyroidectomy (TT) or completion TT were assessed for eligibility and enrolled from Department of Otorhinolaryngology, Head and Neck Surgery and Audiology, Copenhagen University Hospital – Rigshospitalet, Denmark (CUH, $N = 129$) and Department of Otorhinolaryngology and Maxillofacial Surgery, Zealand University Hospital, Køge, Denmark (ZUH, $N = 41$) (Fig. 1). Inclusion criteria were age 18 years or older, clinical indication for primary TT or completion TT, with or without neck dissection. Cases of parathyroid disease or previous parathyroid surgery were excluded. Primary investigator or surgeon enrolled the participants.

Based on a power calculation, with a power of 80%, a level of significance of 5% and an estimated minimal relevant difference in HypoPT of 15% between the two groups, a sample size of 130 patients was calculated. Block-randomization (10 patients in each block) was applied, on each centre separately, using a computer-generated 1:1 model allocating participants into two groups: intervention group (NIR group) and control group (NONIR group), in both of which patients received standard of care thyroidectomy. In the NIR group, PG identification was aided by one of two different NIR imaging camera systems. During dissection the surgeon identified a possible PG with the naked eye and the finding was confirmed or denied by NIR imaging. Additionally, all removed thyroid specimens and the thyroid bed were subsequently inspected with the NIR camera system in attempt to locate PGs in the surgical field or PGs unintentionally removed along with the thyroid gland specimen.

To estimate the PG identification rate, it was assumed that, in each patient, four PGs were present and at risk of damage due to surgery. However, for completion TT in the NIR group, only one neck side had additional NIR imaging and only two PGs were considered at risk.

Autotransplantation was performed if the PG was not viable in situ [30]. Frozen sections were applied in cases when there was doubt if a resected structure represented a PG or not. During every procedure bipolar coagulation and neuromonitoring were used, magnifying surgical loupes were used by surgeon's choice. The surgical light parabol or headlight worn by the surgeons was turned away due to interference with the optical signal.

The patients were blinded with regards to the addition of NIR imaging to their surgery, as were all health care personnel involved in the treatment and evaluation of the patients with the exception, of primary investigator, surgeon, and operating theatre personnel. At CUH and ZUH, seven and three experienced thyroid surgeons, respectively, performed the procedures in both the NIR and the NONIR groups. All surgeons received thorough NIR camera training to avoid a learning curve impacting on results. For the completion TT, the remaining lobe was removed, usually, due to cancer found in the opposite lobe. Importantly, if a completion TT was randomized to the NIR group, the secondary lobectomy was performed with NIR guidance in search of PG. The primary lobectomy had been performed without NIR imaging and thereby, not part of the study. Central or lateral lymph node dissection was performed in cases of thyroid cancer with suspicion of metastases. Soft tissue resection was performed in cases of extrathyroidal invasion. Ionized calcium and parathyroid hormone were measured preoperatively, at 12 h, 1 and 3 months postoperatively. Postoperative ionized calcium as well as symptomatology was primarily used to determine initiation of calcium supplementation. Also, calcium supplementation was initiated if the parathyroid hormone level was reduced by 50% compared with the preoperative result. If ionized calcium levels became lower than 1.00 mmol/L, active vitamin D was added to the treatment. Patients were seen for regular follow-up with a review of medication and blood samples, in the Department of Endocrinology at ZUH or CUH. All blood samples from a particular patient were analyzed at the same laboratory, either CUH or ZUH. Based on the *European Society of Endocrinology Clinical Guideline* [3], the Endocrinologists at CUH and ZUH defined the presence of HypoPT as a result of surgery at timepoints 12 h, 1 and 3 months.

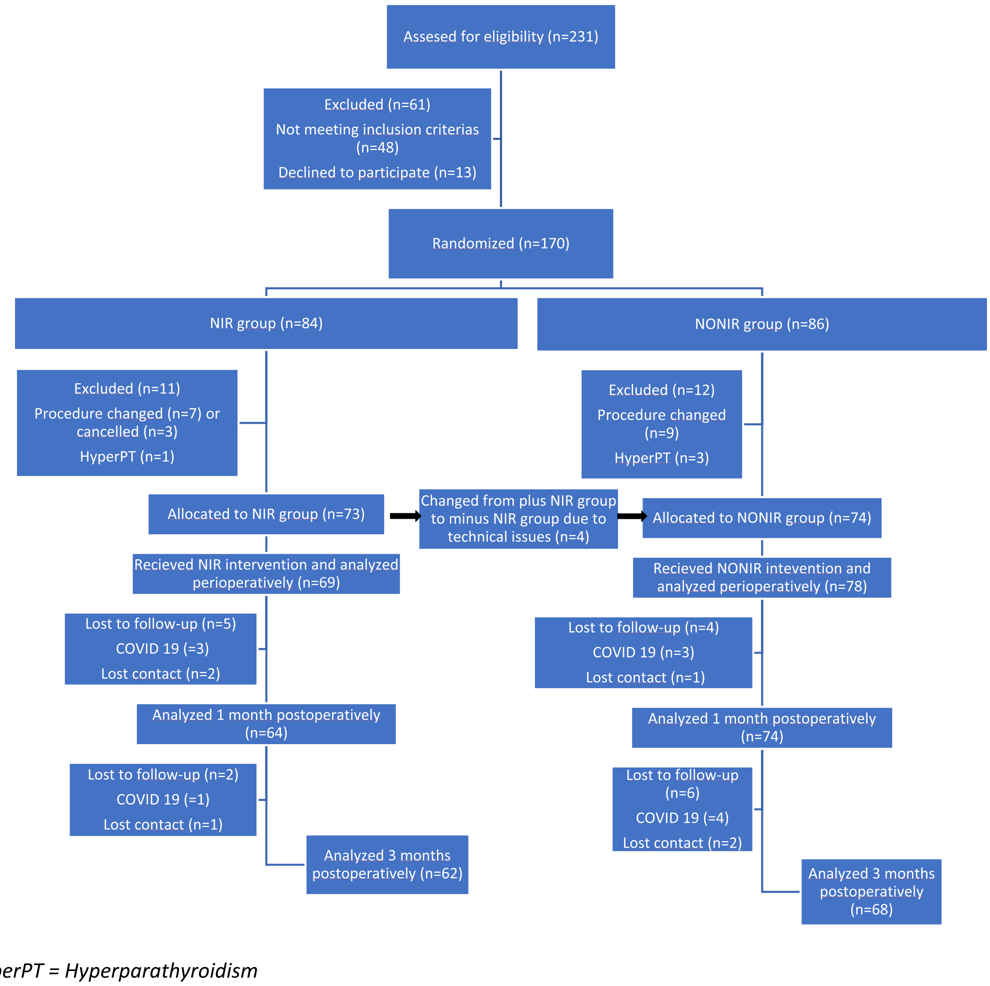

Fig. 1 CONSORT patient flow diagram

For NIR optical guidance, either of two clinically approved camera systems were used, Elevision IR (Stryker, USA) or Fluobeam 800 (Fluoptics, France). Briefly, the Fluobeam 800 consists of a handheld camera with a NIR laser (785 nm) connected to a computer and a screen. The system, which was used in four cases, has a special mode for PG identification and depicts the NIR imaging merged in grey scale video recording in real time. The Elevision IR system generates real-time imaging with a color video recording of the operation field with overlay of the fluorescent signal. The camera head has a NIR laser (805 nm) and is mounted over the surgical field on an adjustable arm. For PG imaging, the system was preset with the Image Profile "Default" and IR Boost was preset to 2.5. In our perception the two camera systems had comparable performance for PG identification and they were chosen since they were accessible in our department for clinical use and research (Fig. 2).

Data collection

Data was collected prospectively and stored in the REDCap database. The primary outcome measure was the rate of HypoPT at timepoints 12 h, 1 and 3 months postoperatively. The secondary outcomes were the PG identification rate, the rate of PGs only identified due to additional NIR imaging and the rate of HypoPT in the NIR group and the NONIR group for the following subgroups: patients with large thyroid glands > 100 g, primary TT, additional lymph node dissection and procedures with a duration exceeding 120 min. Parathyroid hormone was measured with commercially available sandwich electrochemiluminescence immunoassay (ECLIA) at CUH (Roche Diagnostics, Penzberg, Germany) and sandwich chemiluminescence immunoassay at ZUH (Siemens Healthcare Diagnostics Inc., Deerfield, IL, USA). The coefficient of variation was less than 9.8%, and the combined measuring range was 0.6–212 pmol/L.

Statistical analysis

All data were analyzed using the software program R Core Team (2021). For further details, see the Supplementary. Student's *t* test was used for numerical data, while Pearson's chi-squared or Fisher's exact tests were used for categorical data, as appropriate. A two-tailed *p* value of 0.05 was considered statistically significant.

Results

A total of 231 patients with a clinical indication for primary TT or completion TT were assessed for eligibility. Of 170 randomized patients, 84 were allocated to the NIR group and 86 to the NONIR group. Except from age and neck dissection, no statistically significant differences were observed between the two groups at baseline

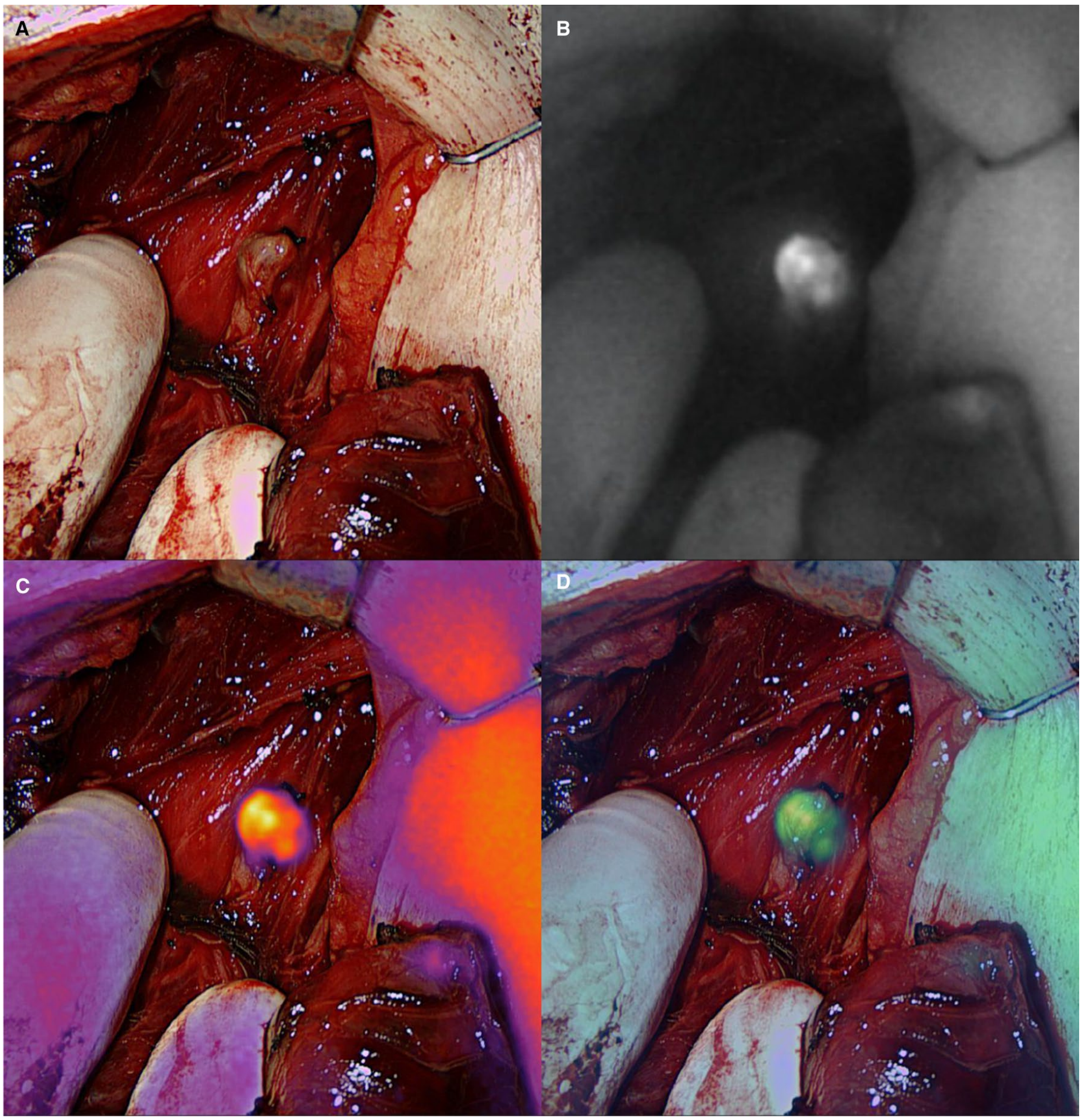

Fig. 2 A parathyroid gland visualized with Elevision IR (Stryker, USA) in four different ways. **A** White light image without any NIR light.**B** Autofluorescent grey scale signal without white light.**C** White light image with merged orange/purple autofluorescent signal representing the parathyroid gland.**D** White light image with merged green autofluorescent signal representing the parathyroid gland

Table 1 Baseline characteristics

Characteristic	Patients, no.		
	NIR group ($n=69$)	NONIR group ($n=78$)	p value
Preoperative variables			
Sex			
Female (%)	50 (72.5)	60 (76.9)	
Male (%)	19 (27.5)	18 (23.1)	0.67
Age mean (sd)	57.4 (16)	52.2 (15.8)	0.05
Tobacco			
Current smoker (%)	10 (14.5)	9 (11.5)	
Never smoker (%)	29 (42.0)	40 (51.3)	
Former smoker (%)	30 (43.5)	29 (37.2)	0.53
BMI mean (sd)	27.2 (4.9)	25.9 (5.4)	0.15
Vitamin D median (IQR)(nmol/L)[a]	63(32.5)	61(32.3)	0.40
Vitamin D > 50 (%)	47 (75.8)	48 (78.7)	0.51
Treatment hospital			
xxxxxxxxxxxxxx CUH (%)	54 (78.3)	52 (66.7)	
Xxxxxxxxxxxxxx ZUH (%)	15 (21.7)	26 (33.3)	0.17
Operative variables			
Histology			
Thyroid cancer (%)	44 (63.8)	44 (56.4)	
Multinodular goiter (%)	18 (26.1)	24 (30.8)	
Graves' disease (%)	3 (4.3)	4 (5.1)	
Follicular adenoma (%)	2 (2.9)	2 (2.6)	
Other (%)	2 (2.9)	4 (5.1)	0.89
Procedure			
Completion thyroidectomy (%)	29 (42.0)	34 (43.6)	
Primary total thyroidectomy (%)	40 (57.9)	44 (56.4)	0.98
Thyroid weight (g) median (IQR)	28 (109)	26 (31)	0.57
Perioperative bleeding (mL) median (IQR)	50 (82)	50 (130)	0.86
Parathyroid reimplantation			
No (%)	61 (88.4)	68 (87.2)	
Yes (%)	5 (7.2)	7 (9.0)	0.94
Neck dissection			
Yes (%)	29 (42.0)	24 (30.8)	
No (%)	40 (58.0)	54 (69.2)	0.21
Central (%)	22 (3.9)	11 (14.1)	
Central + lateral neck (%)	7 (10.1)	13 (16.7)	0.05
Complications to surgery (%)	10 (14.5)	6(7.7)	0.29
Paralysis of the recurrent laryngeal nerve (%)	6 (8.7)	3(3.8)	0.31
Postoperative bleeding (%)	1(1.4)	1(1.3)	
Local wound infection (%)	1(1.4)	1(1.3)	
Reduced function of shoulder (%)	2(2.9)	0	
Chyle leak (%)	1(1.4)	0	

Baseline characteristics and surgical details of patients undergoing primary total thyroidectomy or completion thyroidectomy

BMI body mass index, *n* number

[a]Missing value from 8 patients, 6 NIR and 2 NONIR

Table 2 Postoperative hypoparathyroidism in NIR- and NONIR-group

Characteristic	Patients, no. (%)			
	NIR group	NONIR group	Total	*p* value
Postoperative variables				
Hypoparathyroidism				
Post-operatively (12 h)	$n=69$	$n=78$	$n=147$	0.73
Yes	22 (31.8)	28 (35.9)	50(34.0)	
No	47 (68.1)	50 (64.1)	97 (66.0)	
1-month follow-up	$n=64$	$n=74$	$n=138$	0.50
Yes	9 (14.1)	14 (18.9)	23 (17.7)	
No	55 (86.0)	60 (81.1)	115 (83.3)	
3-months follow-up	$n=62$	$n=68$	$n=130$	0.46
Yes	4 (6.5)	8 (11.8)	12 (9.2)	
No	58 (93.5)	60 (88.2)	118 (90.8)	

Primary outcome (hypoparathyroidism) postoperatively, at 1-month follow-up and at 3- months follow-up

(Table 1). A further description of baseline characteristics is available in the Supplementary.

Table 2 summarizes the overall rate of HypoPT in this cohort at 12 h, 1 month and 3 months, finding rates of 34.0, 17.7, and 9.2%, respectively. There was no significant difference in the rate of HypoPT between the NIR and NONIR groups at the same timepoints.

In the subgroup of patients who underwent a completion thyroidectomy, PTH and ionized calcium prior to the second surgery was within the normal reference interval for all patients, except in one patient in the NONIR group. This patient had a PTH of 9.4 pmol/L and ionized calcium of 1.11 mmol/L after the initial hemithyroidectomy. After the subsequent total thyroidectomy, the initial PTH was 1.11 pmol/L and ionized calcium was 1.09 mmol/L. At 1- and 3-month follow-up the patient remained with hypoparathyroidism.

Results of subgroup analyses are presented in Table 3. No significant differences were observed in either of the subgroups.

Summarized in Table 4, the identification rate of PGs at risk in the NIR group and the NONIR group was 69.5 and 72%, respectively. In the NIR group, 19 PGs (9%) were found only due to NIR imaging. During imaging, a fluorescent signal was detected from a structure not suspected to be a PG, but when surgically explored, a PG appeared visible to the naked eye as well. In four cases, the PG was detected ex vivo when the specimens were searched by imaging. In two of these cases, the PG had a subcapsular location on the thyroid specimen, and in the other two cases, the PG was detected in the resected specimen from a central neck dissection. All identified PGs in the NIR group detected in white light could also be clearly visualized with a NIR signal. Per patient additional PGs was found in 15 patients out of 69 (21.7%).

In the NIR group and the NONIR group, 11 patients (15.9%) and three patients (3.9%), respectively, had a PG unintentionally removed during the procedure.

Discussion

The major finding of the present randomized study was that using NIR imaging during thyroid surgery did not reduce the proportion of patients with HypoPT in the immediate postoperative setting as well as 1 and 3 months postoperatively. This is in line with a recent RCT by Papavramidis et al. [31] who, in a cohort of 180 patients, observed no difference in postoperative hypoparathyroidism incidences between the NIR and NONIR groups (27.7 vs. 25.9%). However, this study conducted only 24 h follow-up compared to 3 months in our study. Similarly, Kim et al. [32], found no statistically significant difference in transient (< 6 months) or permanent hypocalcemia (> 6 months) between NIR (100 cases) and NONIR (200 cases) groups. Serra et al. [33] also reported no difference in 24-h post-operative calcium levels, but a significant improvement in the values of parathyroid hormone at 24 h in the study group. These two studies were both single-surgeon before-and-after studies and consequently there may have been a risk of bias.

A significant difference in postoperative HypoPT between the NIR and NONIR groups has been reported by others: Benmiloud et al. [34] reported significant reduction in transient hypocalcemia (< 6 months) in both a before and after study (NONIR:20.9% vs. NIR:5.3%) and an RCT [35] (NONIR: 21.7 vs. NIR:9.1% $p=0.007$); Kim et al. [36] reported, in a study of 542 patients, significantly lower transient hypoparathyroidism (< 6 months) in the NIR group (NONIR: 46.6 vs. NIR: 33.7%) but no difference in the incidence of hypocalcemia. Dip et al. [37] investigated 170 patients undergoing TT, and observed a nonsignificant 50% postoperative calcium reduction (NONIR: 16.5 vs. NIR:8.2%). Our study observed an unequal distribution for age and neck dissection between NIR and NONIR group. The randomization was performed according to the protocol so we regard this difference as a course of chance.

In our study, the frequency of postoperative HypoPT at 12 h, 1 and 3 months was 34.0, 17.7 and 9.2%, respectively. These results are within the range of other studies and support that the transient HypoPT incidence after primary and completion TT is relatively high and emphasizes that HypoPT is an important health concern for patients subjected to thyroidectomy [1, 6–8, 10]. Study comparison is limited by disagreement on the HypoPT definition and the definition of permanent vs. transient HypoPT. The review paper by Lorente et al.

Table 3 Outcomes in subgroups in NIR- and NONIR-group

Characteristic	Patients, no. (%)		
	NIR group (n = 69)	NONIR group (n = 78)	p value
Primary total thyroidectomy			
Postoperative hypoparathyroidism	N = 40	N = 44	
Yes	18(45)	21 (48)	0.98
Hypoparathyroidism at 1-month follow-up	N = 40	N = 44	
Yes	7 (18)	10 (23)	0.75
Hypoparathyroidism at 3-months follow-up	N = 40	N = 44	
Yes	4 (10.5)	6 (16)	0.74
Large thyroid > 100 g			
Postoperative hypoparathyroidism	N = 19	N = 14	
Yes	6 (32)	5 (36)	1
Hypoparathyroidism at 1-month follow-up	N = 18	N = 13	
Yes	2 (11)	3 (23)	0.63
Hypoparathyroidism at 3-months follow-up	N = 18	N = 10	
Yes	2 (11)	1 (10)	0.63
Neck dissection (central + lateral)			
Postoperative hypoparathyroidism	N = 7	N = 13	
Yes	4 (57)	10 (77)	0.61
Hypoparathyroidism at 1-month follow-up	N = 6	N = 13	
Yes	3 (50)	5 (38.5)	1
Hypoparathyroidism at 3-months follow-up	N = 6	N = 13	
Yes	2 (33)	3 (23)	1
Neck dissection (central)			
Postoperative hypoparathyroidism	N = 22	N = 11	
Yes	9 (41)	4 (36)	1
Hypoparathyroidism at 1-month follow-up	N = 21	N = 11	
Yes	2 (9.5)	2 (18)	0.59
Hypoparathyroidism at 3-months follow-up	N = 19	N = 10	
Yes	1 (5)	2 (20)	0.5
Procedure time > 120 min			
Postoperative hypoparathyroidism	N = 40	N = 39	
Yes	18 (45)	20 (51)	0.74
Hypoparathyroidism at 1-month follow-up	N = 38	N = 37	
Yes	8 (21)	9 (24)	0.95
Hypoparathyroidism at 3-months follow-up	N = 37	N = 33	
Yes	4 (11)	5 (15)	0.73

Subgroup analysis for patients receiving primary total thyroidectomy, patients with large thyroid glands (> 100 g), patients in whom a cervical neck dissection was performed and procedures > 120 min, at 1-month follow-up or at 3-months follow-up. Neck dissection (central + lateral): level 6 plus one or more levels

[4] and the paper by Mehanna et al. [9] highlight these issues and thus the consequences for study comparisons.

Two recent reviews point out the role of low preoperative vitamin D as a predictor for postoperative HypoPT [38, 39] however, only few has low vitamin D as an exclusion criterion [31].

We evaluated the effect of vitamin D status on risk of HypoPT and found no significant effect, which may have been due to lack of sufficient statistical power. We recommend correction of especially vitamin D deficiency before thyroid surgery due to the increased risk of permanent HypoPT in these patients.

In this study 69.5% of the PGs at risk were identified by NIR, which is in the same range as the study by Papavramidis et al. [31], with 66% identified PGs. By the use of NIR imaging prior to dissection, Benmiloud et al. [35] identified 61.6% of PGs before the surgeons could see them. Dip et al. [37] observed no difference in the number of PGs identified

Table 4. Parathyroid identification

Parathyroid glands at risk	Parathyroid glands, no. (%)		
	NIR group ($n=210$)	NONIR group ($n=250$)	Total ($n=460$)
PG identification rate	69.5%	72.0%	
PGs identified in white light and NIR	127	181	326
PGs identified only by NIR	19 (9)	–	–
PGs not identified	64 (30.5)	69 (27.6)	133 (28.9)

Parathyroid glands at risk due to thyroid surgery – primary total thyroidectomy or completion thyroidectomy

PGs parathyroid glands

in the NONIR group after thyroid dissection and the number identified in the NIR group before thyroid dissection. However, the number of PGs identified increased when WL was toggled to NIR imaging.

In our study, 19 PGs appeared with an autofluorescent signal unsuspected by the surgeon and when the camera was focused somewhere else. It is worth noting that, in four of these cases, PGs were identified ex vivo in thyroid gland specimens or neck dissection specimens. These findings emphasize the strength of the additional use of intraoperative NIR imaging to identify PGs that would most likely have remained resected.

A relation between increased risk of HypoPT and the complexity of thyroid surgery has been observed, and NIR autofluorescent PG identification has been proposed as a tool to lower the risk of postoperative HypoPT. Studies have reported neck dissection to be associated with greater risk of developing transient and permanent hypocalcemia [1, 2, 5], and Dedivitis et al. [40] found higher risk of postoperative HypoPT when performing primary TT compared with completion TT. Dip et al. [37] observed, the thyroid gland weight to be predictive of postoperative hypocalcemia. A Danish retrospective review with 602 cases of TT from Sonne-Holm et al. [7] reported a prolonged duration (> 120 min) of surgery to be significantly associated with HypoPT. In our two-centre randomized study of 147 patients and 10 participating surgeons, NIR imaging did not reduce the proportion of HypoPT significantly in the subgroups: patients with large thyroid glands, primary TT, TT and neck dissection or procedure-time > 120 min. This could be due to insufficient power. All the above-mentioned studies included only patients with primary TT performed. In the present study, 29 (42%) patients in the NIR-group had completion TT performed where only one neck side was assessed with NIR imaging in search for PGs, which may have hampered a possible impact of additional use of NIR navigation. However, only one patient in the subgroup of patients who had completion thyroidectomy developed hypoPT following the first surgery. This patient was in the NONIR group and therefore would not impact significantly on the outcomes of this study.

The majority of previous studies have used the Fluobeam 800 system as imaging device. To our knowledge, this is the first study to use the Elevision IR system for PG identification. Both systems deliver a clear fluorescent signal, but Elevision IR has an advantage with the real-time video color imaging of the operating field and the merged fluorescent signal. Both systems are easy to integrate in the operating room setting and are rather easy for surgeons to master after a short learning curve.

When in doubt if a structure is a PG the NIR technique may be essential as a decision tool and thereby influencing the timely workflow of the operation. Also, optical PG imaging may be supportive for the education of less experienced surgeons performing thyroid surgery. Furthermore, frozen section of PGs prior to autotransplantation may be replaced with NIR imaging and reduce procedure time and cost.

The feasibility of the NIR imaging system and ability to find PGs with great certainty is stated by several studies [18–27] However, the technique does not provide information on the blood supply and viability of the glands. This emphasizes the dual challenge; both intraoperative detection and vascularity needs to be evaluated in relation to risk of HypoPT.

Future studies should focus on the utility of NIR light in combination with techniques visualizing sufficient blood supply. The additional use of intravenously injected indocyanine green to evaluate PG vasculature combined with PG NIR autofluorescence imaging has been reported [41]. Intraoperative evaluation of PG vascularization by laser speckle contrast imaging in combination with autofluorescence imaging has also been suggested [42].

Strengths and limitations

The strength of our study is the randomized two-center design including a large cohort of patients undergoing thyroid surgery, conducted by 10 experienced thyroid surgeons with 3 months of follow-up, enabling the evaluation of transient HypoPT. Blinding of the surgical team was not possible. Also, the reported visual identification of a PG relies on a subjective judgement, since histological confirmation is not possible. These issues are a general limitation to this kind of study. Moreover, the heterogeneity of the study population and the fact that a large proportion of the patients had completion TT might compromise the evaluation of a possible effect of NIR PG identification. Seventeen patients were lost to follow-up, of which 11 cases were lost due to the COVID-19 pandemic. Even though the number of patients lost to follow-up is larger than in other studies, we still reached 62 and 68 patients after 3 months in the NIR group and the NONIR group, respectively.

Conclusion

In this study with experienced thyroid surgeons performing thyroidectomy, postoperative HypoPT was less frequent in the NIR group, though not statistically significant, compared with the NONIR group. Autofluorescence-based optical NIR imaging allowed intraoperative identification of PG in thyroid surgery. The identification rate of PGs by use of NIR navigation was 69.5, and in 9% of all PG could be located only due to additional optical imaging. This had an impact on 21,7% patients identification of PG. NIR imaging appears a valuable tool for PG identification and may have a special benefit when applied in complicated thyroid surgery. Further studies are needed.

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Author contributions All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Data availability The data presented in this study are available on request from the corresponding author. The data are not publicly available due to restrictions by the Danish Agency for Data Protection.

Declarations

Conflict of interest Ulla Feldt-Rasmussen's research salary was supported by a grant from The Kirsten and Freddy Johansen's Fund. The authors declare no financial or commercial conflict of interest.

Ethical approval This trial was approved by The Danish National Committee on Health Research Ethics in accordance with the ethical standards of the "Declaration of Helsinki 1964". Approval number: H19010211.

Consent to participate Written informed consent was obtained from all included patients, regarding collecting, saving and publishing their data.

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