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Laryngeal Reinnervation vs Type I Thyroplasty in Unilateral Vocal Fold Paralysis (VOCALIST): A Randomized Feasibility Study

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ABSTRACT

Objectives: We wished to determine the feasibility of performing a multi-centre phase III randomized controlled trial that compares laryngeal reinnervation to type I thyroplasty for adults with unilateral vocal fold paralysis (UVFP) in the UK.

Methods: A feasibility study was designed; 27 participants were recruited at three UK sites. Trial procedures mirrored those intended for a full-scale trial. We assessed recruitment rates, acceptability of randomization, and dropout rates and conducted a qualitative study to understand the recruitment processes. Participants were followed up for up to 12 months to assess optimal outcome measures for the definitive trial covering voice, swallowing, and overall quality of life. A qualitative study was run in parallel with the quantitative clinical trial.

Results: Recruitment was successful with 23 patients with UVFP randomized to reinnervation ($n = 12$) and thyroplasty ($n = 11$). 96% ($n = 22$) of participants accepted the treatment to which they were allocated, of which 17 received their intervention before the study end date. The qualitative study identified minor recruitment challenges that could be addressed through in-trial training. The set of subjective and objective voice, swallowing, and quality of life outcome measures used demonstrated a responsiveness to change following interventions.

Conclusion: The results from this study have provided us with the assurance that conducting an adequately powered randomized controlled clinical trial of laryngeal reinnervation versus type I thyroplasty for adults with UVFP in the UK is feasible in terms of conduct, recruitment, outcome measurement, and completion.

Level of Evidence: 2.

Trial Registration: ISRCTN90201732.

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1 | Introduction

Patients suffering from unilateral vocal fold paralysis (UVFP) exhibit a weak, hoarse voice that fatigues easily [1], with some individuals also experiencing difficulties with breathing and swallowing, whilst failure to achieve a glottic seal reduces the ability to cough and strain effectively. Clearly, the quality of life of affected persons is significantly impacted at home and at work [2, 3].

Speech therapy may suffice, but if not, surgery is considered. Injection of a filler into the paralyzed vocal fold can close the gap temporarily, while more permanent results are achieved surgically with either a static “type 1 thyroplasty” implant or long-term muscle restoration via non-selective laryngeal reinnervation. Type I thyroplasty is held under local anesthetic and lasts approximately 1 h; an opening is created in the cartilage lamina of the larynx allowing a medium grade silastic implant to be inserted and to medialise the paralyzed VF in the midline position. The surgical outcome is the facilitation of the firmer contact of the paralyzed VF with the opposite normal one. Studies reporting surgical outcomes in patients undergoing thyroplasty are limited and often lack robust methodology [4]. Overall, voice is expected to be stronger and more consistent, however, voice improvement may reduce over time due to progressive atrophy of the denervated laryngeal muscles and the effects of normal ageing [5]. Pitch variation may be perceived as suboptimal, since vocal fold tension is not restored by the procedure [6, 7]. On the other hand, non-selective laryngeal reinnervation is a two-hour operation under general anesthesia that aims to restore innervation to the larynx by “borrowing” the activity of other motor nerves. The injured recurrent laryngeal nerve (RLN) and the donor nerve, most commonly the ansa cervicalis, are identified, divided and their ends opposed. The desired surgical outcome is the restoration of the tone and bulk of the vocal folds, enabling pitch control and resulting in a normal or adequately improved voice quality and volume. Both operations are safe and can lead to long-term improvements in glottal closure, preservation of the vibratory vocal fold edge, and notable enhancements in both voice quality and overall quality of life [8, 9].

A systematic review of laryngeal reinnervation studies identified a low quality of existing literature and recommended conducting a formal prospective trial utilizing standardized, internationally recognized outcome measures [10]. Similarly, a systematic review focused on the pediatric population indicated that while surgical management of pediatric bilateral VF palsy leads to subjective symptom improvement, limited data, methodological variability, and inconsistencies in procedural timing and characteristics constrain definitive conclusions regarding the optimal approach [11]. Before committing public resources and patient and staff time to a trial, it's essential to confirm its feasibility and ensure that outcome measures accurately capture objective and subjective voice quality [12, 13]. We therefore conducted a feasibility study to evaluate the practicality of a large, multi-centre phase III RCT comparing reinnervation and type I thyroplasty, with qualitative components to explore recruitment strategies and inform trial design [14].

2 | Materials and Methods

We have previously published the protocol for this feasibility study in full [15] and therefore methods are summarized in

this section. Ethical approval was received from the National Research Ethics Service—Committee Bromley (reference 11/LO/0583).

2.1 | Trial Design

A small version of the proposed future randomized controlled trial (RCT) was set up to recruit up to 30 participants (15 per arm) at 3 recruitment sites in the UK. Sites were chosen on the basis of the Principal Investigators (PIs) having undergone training and subsequent experience in performing reinnervation and thyroplasty surgery.

A qualitative study was run in parallel with the quantitative RCT [Qualitative Research Integrated within Trials (QuinteT) Recruitment Intervention (QRI)] [16].

2.2 | Participants

Potential participants were identified and screened in Ear, Nose and Throat (ENT) outpatient clinics at three UK sites: University College Hospitals NHS Foundation Trust (Royal National Throat Nose and Ear Hospital), University Hospitals Dorset NHS Foundation Trust (Poole Hospital), Manchester University NHS Foundation Trust (Manchester Royal Infirmary). If diagnosed with UVFP in line with the inclusion and exclusion criteria (Table 1), patients were invited to join the study and informed consent was taken.

2.3 | Interventions

Participants allocated to receive laryngeal reinnervation had the surgery under general anesthesia; the injured RLN and the donor nerve were identified and anastomosed. Temporary medialization was given at the time of the surgery to the paralyzed vocal fold by hyaluronic acid (Restylane →, Galderma UK, Watford, UK).

Participants allocated to receive type 1 thyroplasty had the surgery performed under local anesthesia. Medium-grade silastic implants were custom-shaped by the surgeon, with the appropriate size determined intraoperatively using a measuring device. The larynx was assessed in real time through a flexible fiberoptic scope while listening to the patient's voice. In cases where a substantial posterior gap remained that could not be adequately closed using the silastic implant alone, concurrent arytenoid adduction was allowed to address the issue.

Patients were permitted to receive speech and language therapy post-randomization and post-intervention as deemed appropriate by their local multidisciplinary team.

2.4 | Outcomes

Primary and secondary outcome measures were defined in the published protocol, and data collection is summarized in Table 2. The primary outcome focuses on recruitment and

TABLE 1 | Inclusion and exclusion criteria.

Inclusion criteria
1. UVFP due to unilateral recurrent laryngeal nerve paralysis of traumatic, iatrogenic or idiopathic origin of between 6- and 60-months duration, or symptoms that have not sufficiently improved with speech therapy alone, as determined by the patient and agreed by a multidisciplinary clinical team, after 6 months and pending a surgical decision.
2. Age from 18 to 70 years old.
3. Male or female.
4. Able to provide informed consent.
5. A significant voice disorder as measured by perceptual rating (GRBAS Grade ≥ 2) [16] and Voice Handicap Index (VHI-10 score > 16) [17].
6. Common neurophysiological (LEMG) criteria (Koufman Grades 2–5) [18] in either the thyroarytenoid (TA) or posterior cricoarytenoid (PCA) muscle on the paralyzed side.
Exclusion criteria
1. Impaired vocal fold mobility but normal LEMG (Koufman Grade I).
2. Severe lung disorders.
3. Structural vocal fold lesions such as polyp.
4. Previous laryngeal framework surgery.
5. Cricothyroid joint fixation (CAJF).
6. Significant non-laryngeal speech abnormality (severe dysarthria determined by a panel of trained speech therapists).
7. Previous Level 2, 3 or 4 thyroid neck dissection.
8. Previous ipsilateral surgical neck dissection.
9. Previous radiotherapy to the head and neck.
10. Laryngeal injection of a rapidly absorbable material in the last 6 months.
11. Previous laryngeal injection of a non-rapidly absorbable material (e.g., calcium hydroxyapatite).
12. Neuromuscular disease affecting the larynx or multiple cranial nerve palsies.

retention, with secondary outcomes covering voice, swallowing, and quality of life.

2.5 | Sample Size

This study was not formally powered to detect differences between the two interventions. Rather, the sample size was based on Julious [18] who recommends a group size of 12 in order to obtain reasonably precise estimates of an effect and its variance when undertaking a pilot trial without other prior information.

2.6 | Randomization

Participants were allocated to either of the two operations using block randomization stratified by centre. Randomization was

carried out at each site using the web-based service from the company “Sealed Envelope”.

2.7 | Blinding

Due to the nature of the interventions, blinding in this study was limited. Although surgeons and participants were aware of the allocated and conducted intervention, the speech therapist and neurophysiologist outcome raters were blinded.

2.8 | Analytical Methods

Quantitative statistical analyses were conducted by the statistician using STATA 14. Descriptive analyses were used to summarize the characteristics of our sample. An intention-to-treat analysis was performed with the primary and secondary outcomes analyzed descriptively (using either proportions, or means, as appropriate) for each group. Qualitative data analysis involved mapping patient eligibility and recruitment pathways for each centre, reviewing screening and recruitment data, and analyzing staff and patient interviews along with audio recordings of recruitment discussions. Following established QuinteT methodologies [16], interviews and recruitment discussions were audio recorded (with consent), transcribed verbatim, and imported into NVivo 10 (QSR international) data analysis software. Transcripts were coded thematically [19] by an experienced qualitative researcher (SH). Initial themes were discussed and agreed with the senior Qualitative researcher (MJ).

3 | Results

3.1 | Participants Flow

We obtained funding for a period of 24 months to run our small-scale RCT. Twenty-seven people with UVFP were assessed for suitability for the study across the 3 centres (Figure 1). Twenty-three were deemed eligible for enrollment.

3.2 | Baseline Data

Baseline characteristics for age, gender, and ethnicity were evenly matched across the two groups (Table 3) with numbers of surgeries performed at each centre in line with the size and, therefore, expected recruitment and surgery rates of the relevant hospitals.

3.3 | Outcomes and Estimation

3.3.1 | Primary Outcome Measure: Recruitment and Retention

All 23 eligible participants (100%) consented to the study and were randomized, with 12 (53%) randomized to the reinnervation group and $n=11$ (47%) randomized to the thyroplasty group. Of the 23 participants randomized, 17 (74%) received the operation to which they were allocated during the study period.

TABLE 2 | Data collection.

	Screening/ baseline	Follow up				
		2 weeks	2 months	4 months	6 months	12 months
Qualitative audio recordings of staff-patient recruitment conversations	X					
Qualitative research interview*	X		X			
Videostroboscopy**	X				X	X
Laryngeal EMG***	X					X
OperaVOX voice recording	X				X	X
Voice Handicap Index questionnaire (VHI-10) [19]	X				X	X
100mL water swallow test	X				X	X
Eating assessment tool questionnaire (EAT-10)	X				X	X
Health status questionnaire (EQ-5D-5L)	X				X	X
Review of speech and language therapy		X	X	X	X	X
Adverse events		X	X	X	X	X

*QRI interviews took place with patients who have declined randomization up to 1 month after their baseline appointment or with patients who have agreed to randomization at around 2 months post treatment.

**Vocal fold vibration data was graded using the Stroboscopy Research Instrument (SRI) scale, and perceptual voice quality was graded using the GRBAS [18].

***Laryngeal EMG performed at 12 months only in those participants who had undergone reinnervation surgery (LEMG) was anonymised and graded at the end of the study by three independent blinded neurophysiologists using the Koufman grading scale [20].

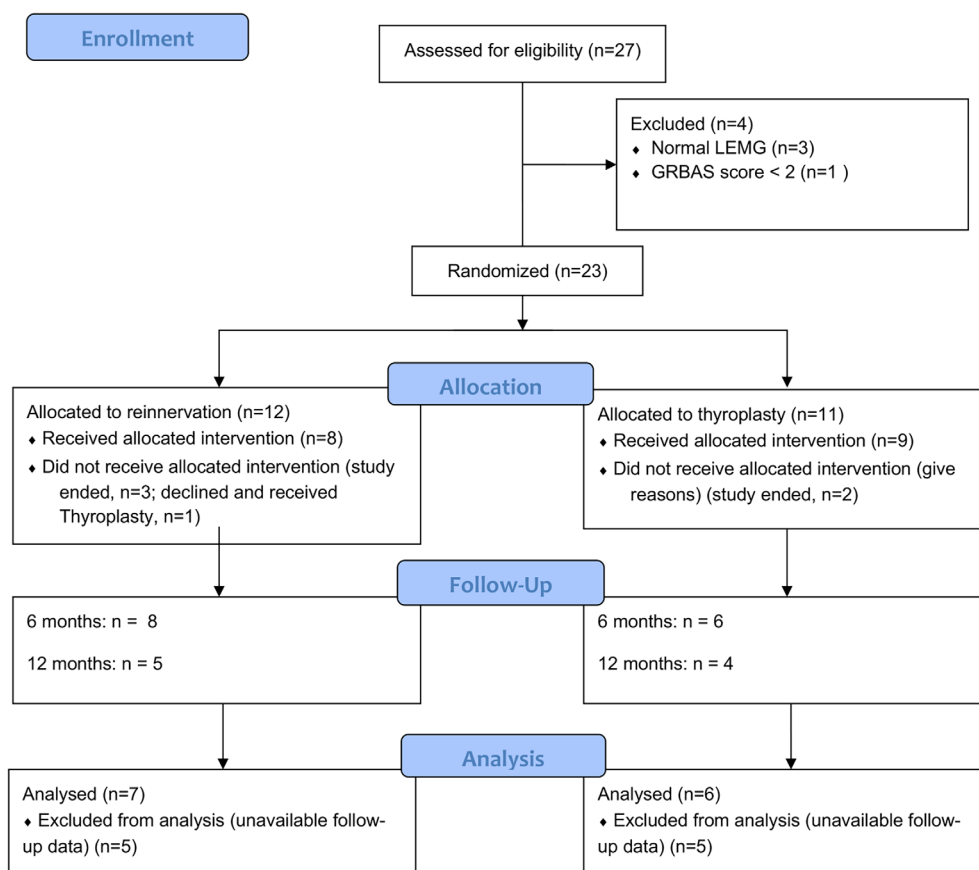

FIGURE 1 | CONSORT flow diagram. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE 3 | Baseline characteristics.

Randomized group		Reinnervation (n = 12)	Thyroplasty (n = 11)
Age (years)		42.75 (13.90)	51.82 (13.52)
Gender	Male	3 (25.0%)	4 (36.4%)
	Female	9 (75.0%)	7 (63.6%)
Ethnicity	White (British)	9 (75.0%)	10 (90.9%)
	Asian (Indian)	0 (0%)	1 (9.1%)
	Black (African)	1 (8.3%)	0 (0%)
	Other (not know)	1 (8.3%)	0 (0%)
	Other (not stated)	1 (8.3%)	0 (0%)
Site	UCLH	5 (41.7%)	2 (18.2%)
	CMFT	5 (41.7%)	7 (63.6%)
	PFHT	2 (16.7%)	2 (18.2%)
EQ-5D-5L		0.78 (0.26)	0.65 (0.29)
VHI-10		28.00 (4.13)	30.55 (7.16)
EAT-10		15.67 (11.97)	13.27 (10.73)
GRBAS: G		1.92 (0.94)	2.12 (0.76)
GRBAS: R		1.28 (0.69)	1.33 (0.82)
GRBAS: B		0.47 (0.76)	0.33 (0.47)
GRBAS: B		1.58 (1.06)	1.88 (0.85)
GRBAS: S		1.11 (1.44)	0.85 (0.89)
Swallow volume (mL)		12.64 (4.23)	13.65 (7.25)
Swallow capacity (mL/s)		7.66 (5.86)	7.65 (7.10)
Swallow speed (s)		2.59 (2.45)	2.19 (1.04)
Jitter*		4.84 (2.98)	6.24 (3.77)
Shimmer*		10.67 (5.83)	10.92 (4.89)
ShimmerdB*		1.41 (0.87)	1.60 (0.98)
Noise/harmonic ratio*		0.42 (0.53)	0.80 (0.82)
Harmonic/noise ratio*		11.89 (3.47)	9.53 (7.52)
Fo (Hz)*		203.11 (40.44)	199.06 (25.58)
Maximum phonation time (s)		5.41 (3.56)	4.45 (2.49)
Pitch range (speaking) (Hz)		177.97 (197.19)	219.51 (153.83)

Note: Values are mean (Sd) or N (%).

*1 missing value for reinnervation group.

One participant declined to receive the reinnervation surgery to which they were allocated and withdrew from the study, citing their familiarity with a previous case of successful thyroplasty, which influenced their treatment preference. In one participant undergoing reinnervation surgery, it was found at the time of surgery that it was not possible to perform reinnervation due to excessive scarring, and so the operation was converted to thyroplasty. This participant remained in the study and their data were included in the reinnervation group as per the intention to treat analysis plan.

Due to the time restraints of the study, and that the recruitment period continued up until the end of the study time period, five patients had surgery later than 6 months before the end of the study, while five patients did not receive surgery within the timeframe of the trial. Consequently, although we included them in the qualitative analysis, they could not be followed up for their 6- and 12-month appointments. As a result, they are noted here as lost to follow up and their 6- and 12-month voice quality data did not make part of the quantitative secondary analysis. However, these patients were followed up according

to the post-operative monitoring regular NHS procedures, outside the context of this trial. Thirteen participants (7 from the innervation group) were included in the quantitative analysis. Thirteen patients had 6-month values, of which 8 also had 12-month values.

The QuinteT Recruitment Intervention (QRI) assessment of recruitment within this feasibility study was successfully completed. Audio recordings were received from initial consultations with 21 patients across all three sites. Of the 7 trial staff members approached for interview, six interviews were conducted and analyzed, including the trial manager, chief investigator, recruiting surgeons, and research nurses across the centres. One staff member was unavailable for interview. Interviews were carried out by SH over the telephone and lasted on average 52 min (range 22–75 min). All three patients approached for interview agreed to participate. See Supporting Information 1 for full QRI data set.

In their interviews, staff (PI surgeons) indicated a commitment to the study and a willingness to recruit patients to a main study in order to better inform their practice. However, some highlighted that the arbitrary nature of some of the eligibility criteria may narrow the pool of potentially eligible patients, citing examples of people whose age was outside the inclusion criteria, whose VHI score was too low, or those who had UVFP for too long. It was suggested that expanding these criteria may help increase the pool of eligible patients.

Whilst willing to recruit patients to VOCALIST, there was a preference among some treating clinicians for reinnervation over Thyroplasty. This preference was also apparent in recordings of recruitment consultations, with recruiters often spending longer presenting information about reinnervation and spending more time outlining the disadvantages of Thyroplasty. This could shape patient preferences towards reinnervation and

discourage them from considering randomization. A summary of the main topics identified from QRI, and the trial areas that were improved or could be improved in a subsequent full-scale RCT are shown in Table 4.

3.3.2 | Secondary Outcome Measures

3.3.2.1 | General Health Status. The patient-rated EQ-5D-5L captured the overall health status of participants in both groups following intervention, and the results are provided in detail in Supporting Information 2.

3.3.2.2 | Voice Outcome Measurements. Voice outcome measurements were successfully obtained from participants covering four multidimensional domains:

3.3.2.2.1 | Self-Perception—Self-Rated Questionnaire. VHI-10 data was collected at baseline ($N=23$, 11 from the thyroplasty and 12 from the reinnervation group), and then at 6 ($N=13$, 6 from the thyroplasty and 7 from the reinnervation group) and 12 months post-operatively ($N=9$, 4 from the thyroplasty and 5 from the reinnervation group). VHI-10 detected a clinically significant positive change (6 or more points [20]) in the participants' perception of their dysphonia following both interventions at 6 and 12 months (Table 5). All participants showed improvement in their VHI-10 score when comparing their final values to baseline [18], with the exception of one patient in the reinnervation group (Supporting Information 3).

3.3.2.2.2 | Auditory-Perceptual; GRBAS Four-Point Grading Scale. Independent GRBAS grading were conducted by three independent blinded speech and language therapists (Table 6) with appropriate inter-rater reliability; G 0.982 (0.972 to 0.990); R 0.972 (0.955 to 0.984); B 0.984 (0.975 to 0.991); A

TABLE 4 | Main themes extracted from qualitative study analysis with mitigations.

Area of trial	Theme	Data source(s)	Mitigation
Study introduction	Introduction in an open area such as waiting room felt to be too impersonal	Staff interviews/ Patient interviews	Identification of private rooms/areas for discussions with potential recruits.
Surgical variation	Differences in clinical decision regarding offering/use of temporary injections	Staff interviews	Here, we pragmatically left this decision to individual surgeons, but clarity and uniformity may be better in a full RCT.
Consenting	Some participants perceived imbalances/bias in the way the two arms were presented.	Consultation recordings/ Patient interviews	Overcome by staff training to maintain clinical and trial staff equipoise.
	Some patients presented with preconceptions regarding treatment preferences.	Consultation recordings	Training from QRI encouraged trial staff to explore these preferences in depth to ensure both patients were making informed decisions.
	The concept of randomization was difficult for some trial staff to explain.	Consultation recordings/ staff interviews	This was overcome with further training.

TABLE 5 | VHI-10 mean scores.

	Baseline (SD)	<i>n</i>	6 months (SD)	<i>n</i>	12 months (SD)	<i>n</i>
Type I thyroplasty	30.55 (7.16)	11	4.17 (4.96)	6	2.50 (3.70)	4
Laryngeal reinnervation	28.00 (4.13)	12	17.13 (11.53)	7	15.60 (11.08)	5

TABLE 6 | GRBAS mean scores.

	Baseline (SD)	<i>n</i>	6 months (SD)	<i>n</i>	12 months (SD)	<i>n</i>
G						
Type 1 thyroplasty	2.12 (0.76)	11	0.78 (0.75)	6	0.75 (0.50)	4
Laryngeal reinnervation	1.92 (0.94)	12	1.57 (0.79)	7	1.25 (1.50)	4
R						
Type 1 thyroplasty	1.33 (0.82)	11	0.50 (0.84)	6	0.75 (0.50)	4
Laryngeal reinnervation	1.28 (0.69)	12	1.10 (0.60)	7	1.00 (1.15)	4
B						
Type 1 thyroplasty	1.88 (0.85)	11	0.50 (0.55)	6	0.33 (0.47)	4
Laryngeal reinnervation	1.58 (1.06)	12	1.00 (1.15)	7	1.08 (1.42)	4
A						
Type 1 thyroplasty	0.33 (0.47)	11	0.06 (0.14)	6	0.17 (0.33)	4
Laryngeal reinnervation	0.47 (0.76)	12	0.29 (0.62)	7	0.92 (1.07)	4
S						
Type 1 thyroplasty	0.85 (0.89)	11	0.06 (0.14)	6	0.00 (0.00)	4
Laryngeal reinnervation	1.11 (1.44)	12	0.76 (0.98)	7	0.67 (1.12)	4

Abbreviations: A, asthenia & strain; B, breathiness; G, grade; R, roughness.

0.874 (0.797 to 0.925); and S 0.986 (0.977 to 0.992). Both treatment groups displayed a trend of improvement for the measures of grade (G), roughness (R), breathiness (B) and strain (S) over the time period of the study.

3.3.2.2.3 | Acoustic Voice Quality—“On Person Rapid Voice Examiner”. Acoustic measurements were obtained from the portable OperaVOX device for Jitter, Shimmer, Noise-to-harmonic ratio (NHR), Harmonic-to-noise ratio (HNR), Fundamental frequency (F0) and Pitch range and are provided in Supporting Information 4.

3.3.2.2.4 | Aerodynamic Voice Measurements. Maximum Phonation Time (MPT) obtained from the portable OperaVOX device detected an increase in glottic efficiency following the interventions. In the Type 1 Thyroplasty group, mean MPT was found 4.45 (2.49), 9.70 (5.96), and 14.14 (12.37) at baseline, 6 and 12 months respectively. In the reinnervation group, mean MPT was found 5.41 (3.56), 7.46 (5.35), and 7.81 (5.54) at baseline, 6 and 12 months respectively.

3.3.2.3 | Physical Laryngeal Outcome Measurements. Vocal fold vibration data, collected using videostroboscopy and graded by three independent blinded raters using the SRI scale, were insufficient for analysis due to numerous

missing values, which compromised the dataset's integrity and interpretability.

Laryngeal electromyography (EMG) was used to evaluate the integrity of the neuromuscular system in the larynx. Three blinded neurophysiologists graded the pre-operative data using the Koufman and Walker grading scale (Supporting Information 5). Data collected at 12 months in the laryngeal reinnervation participants displayed an improvement in innervation over what was already present pre-operatively (Supporting Information 6).

3.3.2.4 | Swallowing Outcome Measurements. Scores from the patient-rated EAT-10 questionnaires and the 100 mL water swallow test (Table 7) captured clinically significant improvements in participants' swallowing following intervention. All participants improved their swallow volume, with the exception of one patient in the reinnervation group and 3 in the thyroplasty group (Supporting Information 7).

3.4 | Safety

In the reinnervation group (*n* = 12) there were 22 adverse events (AEs) recorded, with 1 participant having 1 serious adverse event (SAE: DVT and pulmonary embolism). In the thyroplasty

TABLE 7 | Swallowing outcome measurements.

	Baseline (SD)	<i>n</i>	6 months (SD)	<i>n</i>	12 months (SD)	<i>n</i>
EAT-10 score						
Type 1 thyroplasty	13.27 (10.73)	11	2.83 (5.12)	6	5.00 (10.00)	4
Laryngeal reinnervation	15.67 (11.97)	12	8.25 (8.80)	8	14.00 (9.41)	5
Swallow volume (mL)						
Type 1 thyroplasty	13.65 (7.25)	11	17.35 (8.70)	6	16.81 (6.89)	4
Laryngeal reinnervation	12.64 (4.23)	12	19.72 (8.58)	7	20.36 (9.40)	4
Swallow speed (sec)						
Type 1 thyroplasty	2.19 (1.04)	11	1.64 (0.32)	6	1.77 (0.28)	4
Laryngeal reinnervation	2.59 (2.45)	12	2.48 (0.93)	7	3.09 (1.45)	4
Swallow capacity (mL/s)						
Type 1 thyroplasty	7.65 (7.10)	11	10.92 (5.57)	6	10.07 (5.48)	4
Laryngeal reinnervation	7.66 (5.86)	12	7.87 (1.20)	7	6.64 (0.54)	4

group ($n = 11$), there were 21 AEs, and 1 participant had 2 SAEs (chest infection and hospitalization).

4 | Discussion

4.1 | Strengths and Limitations

VOCALIST is the first feasibility clinical trial to provide reliable information on how to conduct a future multi-centre trial in the UK to test and compare the effectiveness of two surgical approaches for restoration of laryngeal function in adults with UVFP. It has been developed to address an identified knowledge gap, which has become increasingly apparent not only in everyday clinical practice but also in the existing literature; a systematic review highlighted the inadequacy of current research on laryngeal Reinnervation and Thyroplasty, pointing to the overall low quality of available studies. This gap in knowledge underscored the need for a formal prospective trial, utilizing standardized outcome measures, to provide more reliable and clinically relevant data [10].

In our knowledge, to date, the only published randomized clinical trial comparing the results of Thyroplasty and Reinnervation in UVFP was conducted more than 10 years ago in the USA [12]. The study was reported to have been suspended prematurely because of informed consent irregularities and slow accrual at several sites. Although it concluded that there was no significant difference between the Thyroplasty and reinnervation groups, the study was underpowered with 24 participants from 9 clinical sites.

In view of the challenges associated with recruiting to a phase III surgical study of this type, we aimed to gain as much insight as possible from this previous feasibility trial prior to running a larger scale phase III RCT. In order to achieve this goal, a rigorous study design that takes into account objective and subjective voice and swallowing outcome measures was implemented. Furthermore, a multidisciplinary team and UVFP patients were

engaged throughout the design, setup, analysis, and dissemination phases of the feasibility study.

This study has some limitations. Surgeons' preference, values or experience may affect all study phases, from patients' recruitment and counseling to data collection, analysis, and interpretation [17]. To overcome operators' bias, we included multiple surgeons from different institutions, and the included participants were randomly assigned to the two interventions. Moreover, although the nature of treatment made it difficult to blind participants and study personnel, all postoperative voice assessments and functional outcomes were evaluated by observers blinded to the surgical technique (speech therapists, neurophysiologists).

Another limitation is that, to date, few ENT surgeons in the UK are trained to perform laryngeal reinnervation, and so our study was limited to recruiting at those UK sites where surgeons had significant (> 10 cases) operative experience. This may limit the generalizability of our findings, but it ensures that a future adequately powered clinical trial may safely be conducted by the same scientific team in these same 3 UK clinical centres, extending to other centres as further surgeons are trained. Finally, whilst we were aiming to follow up all participants for 12 months, budget and time constraints, the overlap between recruitment and study closure, and the necessity of meeting the trial's endpoint necessarily limited the duration of follow-up for some of the participants recruited later in the study, such that only a small sample of potential data could be usefully analyzed. An intention-to-treat analysis was conducted, and missing data are, by chance, equally distributed between the two groups, something that may minimize the effect of attrition bias. Long-term (12-month) data remains limited, and short-term results should be interpreted with caution. The expected physiological timeline for nerve regeneration extends well beyond 6 months, meaning that improvements will still be evolving for a year or more, whilst shorter-term results are confounded by the effects of concurrent injection laryngoplasty. Similarly, for thyroplasty, early post-surgical voice outcomes may not fully reflect

long-term stability, as tissue and scar remodeling and muscle wasting continue over time. This highlights a well-recognized challenge in trials of surgical interventions with variable scheduling and recovery periods.

4.2 | Generalizability

With 85% of screened patients eligible, this feasibility study informs future trial design. Due to budget and time limits, some participants were only followed under standard clinical care, but in a large-scale RCT, extending recruitment and monitoring would allow complete data collection. Expanding to more clinical centers, with UK surgeons trained in laryngeal reinnervation, would also support recruitment.

In view of our experience gained during this feasibility study, in future studies we may focus on a shorter list of objective and subjective outcomes to improve the power of the analysis and to be comparable with literature (i.e., VHI-10 as primary outcome, and GRBAS and EMG as secondary ones). In the present study, both interventions showed variable but overall positive improvements in voice and swallowing, with adverse events comparable to literature [21–23]. Confounding factors, such as concurrent injection laryngoplasty and speech therapy, should be addressed in future studies to ensure consistency across groups.

The adverse events reported in our feasibility study are within the range of those mentioned in the existing literature for similar surgical interventions [24, 25]. A recent systematic review encompassing 2426 patients undergoing type 1 thyroplasty reported an overall complication rate of 10.5% (major complications 4.5%) [24]. Similarly low are the reported complications associated with reinnervation (6.8% according to a recent meta-analysis of 132 patients) [25]. All this suggests that the safety profiles of both thyroplasty and laryngeal reinnervation are acceptable and do not differ greatly, supporting the feasibility of comparison in a future adequately powered clinical trial.

5 | Conclusions

Any comparison of the results between the two interventions was out of the scope of this study, which is a feasibility study and is therefore underpowered. Nevertheless, important observations have been made, and the insights gained in this feasibility study will contribute to the successful design and implementation of a future RCT.

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Conflicts of Interest

Martin Birchall acts as Consultant to Altavo GMBH. The other authors declare no conflicts of interest.

References

1. S. Misono and A. L. Merati, "Evidence-Based Practice: Evaluation and Management of Unilateral Vocal Fold Paralysis," *Otolaryngologic Clinics of North America* 45, no. 5 (2012): 1083–1108, <https://doi.org/10.1016/j.otc.2012.06.011>.
2. T. J. Fang, H. Y. Li, R. E. Gliklich, Y. H. Chen, P. C. Wang, and H. F. Chuang, "Quality of Life Measures and Predictors for Adults With Unilateral Vocal Cord Paralysis," *Laryngoscope* 118, no. 10 (2008): 1837–1841, <https://doi.org/10.1097/MLG.0b013e31817e7431>.
3. M. E. Smith, L. O. Ramig, C. Dromey, K. S. Perez, and R. Samandari, "Intensive Voice Treatment in Parkinson Disease: Laryngostroboscopic Findings," *Journal of Voice* 9, no. 4 (1995): 453–459, [https://doi.org/10.1016/s0892-1997\(05\)80210-3](https://doi.org/10.1016/s0892-1997(05)80210-3).
4. D. S. Lundy, R. R. Casiano, J. W. Xue, and F. L. Lu, "Thyroplasty Type I: Short- Versus Long-Term Results," *Otolaryngology-Head & Neck Surgery* 122, no. 4 (2000): 533–536, <https://doi.org/10.1067/mhn.2000.102186>.
5. T. D. Anderson, J. R. Spiegel, and R. T. Sataloff, "Thyroplasty Revisions: Frequency and Predictive Factors," *Journal of Voice* 17, no. 3 (2003): 442–448, [https://doi.org/10.1067/s0892-1997\(03\)00080-8](https://doi.org/10.1067/s0892-1997(03)00080-8).
6. N. Maronian, P. Waugh, L. Robinson, and A. Hillel, "Electromyographic Findings in Recurrent Laryngeal Nerve Reinnervation," *Annals of Otolaryngology, Rhinology, and Laryngology* 112, no. 4 (2003): 314–323, <https://doi.org/10.1177/000348940311200405>.
7. V. Uloza, R. Pribušiene, and V. Saferis, "Multidimensional Assessment of Functional Outcomes of Medialization Thyroplasty," *European Archives of Oto-Rhino-Laryngology* 262, no. 8 (2005): 616–621, <https://doi.org/10.1007/s00405-004-0755-7>.
8. W. Wang, D. Chen, S. Chen, et al., "Laryngeal Reinnervation Using Ansa Cervicalis for Thyroid Surgery-Related Unilateral Vocal Fold Paralysis: A Long-Term Outcome Analysis of 237 Cases," *PLoS One* 6, no. 4 (2011): e19128, <https://doi.org/10.1371/journal.pone.0019128>.
9. A. D. Schuman, G. A. Calderara, A. Hanif, S. Hollas, and J. Ongkasuwan, "Long-Term Outcomes of Pediatric Laryngeal Reinnervation," *Laryngoscope* 134, no. 12 (2024): 5006–5009, <https://doi.org/10.1002/lary.31667>.
10. B. B. Aynehchi, E. D. McCoul, and K. Sundaram, "Systematic Review of Laryngeal Reinnervation Techniques," *Otolaryngology - Head & Neck Surgery* 143, no. 6 (2010): 749–759, <https://doi.org/10.1016/j.otohns.2010.09.031>.
11. N. Nemry and J. R. Lechien, "Surgical Treatments of Pediatric Bilateral Vocal Fold Paralysis: A Systematic Review," *Journal of Otolaryngology - Head & Neck Surgery* 53 (2024): 19160216241291807, <https://doi.org/10.1177/19160216241291807>.
12. R. C. Paniello, J. D. Edgar, D. Kallogjeri, and J. F. Piccirillo, "Medialization vs. Reinnervation for Unilateral Vocal Fold Paralysis: A Multicenter Randomized Clinical Trial," *Laryngoscope* 121, no. 10 (2011): 2172–2179, <https://doi.org/10.1002/lary.21754>.
13. M. Mat Baki, R. Yu, J. S. Rubin, E. Chevreton, G. Sandhu, and M. A. Birchall, "Patient Perception of a Randomised, Controlled Trial of Laryngeal Reinnervation Versus Thyroplasty for Unilateral Vocal Fold Paralysis," *Journal of Laryngology and Otolaryngology* 129, no. 7 (2015): 693–701, <https://doi.org/10.1017/S0022215115000985>.
14. R. C. Stein, J. A. Dunn, J. M. Bartlett, et al., "OPTIMA Prelim: A Randomised Feasibility Study of Personalised Care in the Treatment of Women With Early Breast Cancer," *Health Technology Assessment* 20, no. 10 (2016): 1–202, <https://doi.org/10.3310/hta20100>.

15. H. Blackshaw, P. Carding, M. Jepson, et al., “Does Laryngeal Reinnervation or Type I Thyroplasty Give Better Voice Results for Patients With Unilateral Vocal Fold Paralysis (VOCALIST): Study Protocol for a Feasibility Randomised Controlled Trial,” *BMJ Open* 7, no. 9 (2017): e016871, <https://doi.org/10.1136/bmjopen-2017-016871>.
16. J. L. Donovan, L. Rooshenas, M. Jepson, et al., “Optimising Recruitment and Informed Consent in Randomised Controlled Trials: The Development and Implementation of the Quintet Recruitment Intervention (QRI),” *Trials* 17, no. 1 (2016): 283, <https://doi.org/10.1186/s13063-016-1391-4>.
17. B. A. Armstrong, I. A. Dutescu, A. Tung, et al., “Cognitive Biases in Surgery: Systematic Review,” *British Journal of Surgery* 110, no. 6 (2023): 645–654, <https://doi.org/10.1093/bjs/znad004>.
18. C. A. Rosen, A. S. Lee, J. Osborne, T. Zullo, and T. Murry, “Development and Validation of the Voice Handicap Index-10,” *Laryngoscope* 114, no. 9 (2004): 1549–1556, <https://doi.org/10.1097/00005537-200409000-00009>.
19. V. Braun and V. Clarke, “Using Thematic Analysis in Psychology,” *Qualitative Research in Psychology* 3 (2006): 77–101, <https://doi.org/10.1191/1478088706qp0630a>.
20. S. Misono, B. Yueh, A. N. Stockness, M. E. House, and S. Marmor, “Minimal Important Difference in Voice Handicap Index-10,” *JAMA Otolaryngology. Head & Neck Surgery* 143, no. 11 (2017): 1098–1103, <https://doi.org/10.1001/jamaoto.2017.1621>.
21. I. Kissel, L. K. Van, E. D’haeseleer, et al., “Longitudinal Vocal Outcomes and Voice-Related Quality of Life After Selective Bilateral Laryngeal Reinnervation: A Case Study,” *Journal of Speech, Language, and Hearing Research* 66, no. 1 (2023): 1–15, https://doi.org/10.1044/2022_JSLHR-22-00398.
22. L. A. DiNardo, M. Rosi-Schumacher, C. C. Kuo, R. Nagy, and M. M. Carr, “An Analysis of Postoperative Complications in Medialization Thyroplasty: NSQIP Data,” *ORL J Oto-Rhino-Laryngol Its Relat Spec* 85, no. 1 (2023): 20–27, <https://doi.org/10.1159/000526282>.
23. M. B. Marina, J. P. Marie, and M. A. Birchall, “Laryngeal Reinnervation for Bilateral Vocal Fold Paralysis,” *Current Opinion in Otolaryngology & Head and Neck Surgery* 19, no. 6 (2011): 434–438, <https://doi.org/10.1097/MOO.0b013e32834c7d30>.
24. V. F. Torrecillas, M. R. Hoffman, B. Schiffer, K. Keefe, and M. E. Smith, “Long-Term Outcomes and Revision Rates in Laryngeal Reinnervation,” *Laryngoscope* 134, no. 7 (2024): 3187–3192, <https://doi.org/10.1002/lary.31297>.
25. Z. A. Valley, A. Karp, and D. Garber, “Safety and Adverse Events of Medialization Thyroplasty: A Systematic Review,” *Laryngoscope* 134, no. 5 (2024): 1994–2004, <https://doi.org/10.1002/lary.31141>.

Supporting Information

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