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CORSO DI DOTTORATO DI RICERCA IN

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CICLO ***XXV***

TESI DI DOTTORATO DI RICERCA

Study design and development of a new technique for percutaneous dilatational tracheostomy called G-Trach.

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Summary

Tracheostomies are currently used for airway management in patients requiring long-term respiratory assistance, the dilatational percutaneous technique being a valuable alternative to traditional surgical ‘open’ techniques. In this study, we developed a novel dilatational percutaneous tracheostomy device using a balloon dilator with a particular innovative shape (G-Trach). We tested, this device, at the Autonomous University of Barcelona Veterinary Institute, on eight pigs (weighing 20–40 kg) which were anaesthetised and underwent tracheostomy using the novel G-Trach technique. The mean (SD) procedure time was 2.63(0.64) min from tracheal puncture to ventilation through the tracheostomy tube; the mean (SD) time from positioning the dilator balloon to introducing the cannula was 0.71(0.38) min. Vital functions and oxygen saturation remained constant throughout the procedures. Post-mortem examinations did not reveal any tracheal injury. Thus, the G-Trach seems to be a safe and easy new dilatational percutaneous technique for forming tracheostomies. A preliminary study on humans (six patients) confirmed the results of the study on pigs and has shown the need of some changes to the device to improve the transition between the balloon and the distal part of the tube tracheotomy. A new patent request has therefore been submitted wherein the profile of the balloon (shaped as an inverted cone) is prolonged so as to wrap the tip of the tracheostomy tube.

Introduction

Over the past 20 years there has been a rapid growth in the use of tracheostomies for the management of patients requiring long-term respiratory assistance in intensive care units (ICUs) [10,12,15]. The reasons that have led to a growth of this procedure have been investigated by means of numerous randomized clinical trials. A plausible reason would appear to be a facilitated weaning thanks to a reduced work of breathing (WOB) because of a decrease in flow resistance. Indeed, in a laboratory study, Davis et al. [8] showed that, under all investigated conditions, WOB was lower with a tracheostomy tube than with an endotracheal tube of equivalent internal diameter, a difference that increased with increasing inspiratory flows. The same investigators confirmed this in vivo and also showed that intrinsic positive end-expiratory pressure (PEEP) was slightly reduced after tracheotomy [8]. These effects were even more pronounced in a population of COPD patients that failed weaning, in which case, during spontaneous breathing at different levels of pressure support, marked decreases in intrinsic PEEP and WOB were observed [11].

Endotracheal intubation can result in severe injury of the upper airways [6] which can be largely prevented by early tracheotomy. Tracheotomy improves nutrition, mobility and speech, clearance of secretion and patient comfort. In an observational study, tracheotomised mechanically ventilated ICU patients required less intravenous administration of sedatives [20]. In addition, patients can be nursed outside intensive care unit (ICU) and the timing of tracheostomy may favourably influence the time of weaning, thus leading to a reduced hospitalisation period in the ICU [15, 21]. Moller and coworkers [19] found that patients requiring prolonged mechanical ventilation had a lower incidence of ventilator-associated pneumonia, a shorter ventilator time, and lower hospitalisation periods in the ICU, when tracheostomy was performed within 7 days after admission to the surgical ICU. Similar findings were reported by Arabi and co-workers [2].These, however, are observational studies; hence, the reported findings are ranked grade B evidence.

Numerous studies have tested low-invasive surgical, percutaneous and trans-laryngeal techniques to identify safe, efficient and convenient alternatives to the standard ‘open’ surgical tracheostomy [1,3,4,13,14,16,18] The operative complications of PDT(percutaneous dilatational tracheostomy) and ST(surgical tracheostomy) and their reported frequencies are summarized in Table 1.

Table.1 Descriptions and Frequencies (% in brackets) of Operative Complications of PDT and ST in four different trials (n. numbers of observations), as from the indicated references.

Complications	Friedman et al (13)		Holdgaard et al (16)		Sushil P. Ambesh (1)	F. Beltrame et al (3)	
	PDT n.26	ST n.27	PDT n.30	STn.30	PDT n.60	PDT n.367	ST n.161
Major bleeding†				2 (7%)			8 (4,9%)
Minor bleeding*	3 (13%)	3 (11%)	6(20%)	24(80%)	6 (10%)		3 (1,8%)
Hypoxia***		3 (11%)				6 (1,6%)	2 (1,2%)
Paratracheal insertion	1(4%)						
Hypotension****	4 (15%)	3 (11%)			2 (3%)	4 (1%)	2 (1,2)
Loss of airway (>20 s)		1 (4%)					
Resistance to insertion			8(27%)		11 (18%)		
Cuff puncture			5(17%)				
Surgical emphysema		1 (4%)			3 (5%)		
Pneumothorax					1 (1,6%)		
Tracheal mucosa lacerations/abrasions					5 (8%)		
Rupture of cricoid or tracheal rings.**					9 (15%)	35(9,5%)	
Accidental extubation					1 (1,6%)	9 (2,5%)	3 (1,8%)
other	4 (15%)						13 (12,3%)
Total	12/26 (47%)	11/27 (40%)	19/30 (63%)	26/30 (86%)	38/60 (63%)	54/367 (14,6%)	31/161 (19,2%)

*In the PDT group, minor bleeding was defined as bleeding that could be controlled by digital pressure. In the SCT group, minor bleeding was defined as bleeding controlled by electrocautery.

†In the PDT group, major bleeding was defined as bleeding that required additional measures to control. In the SCT group, major bleeding was defined as bleeding sufficient to obscure the operative field, or which required suture ligature to control(16)

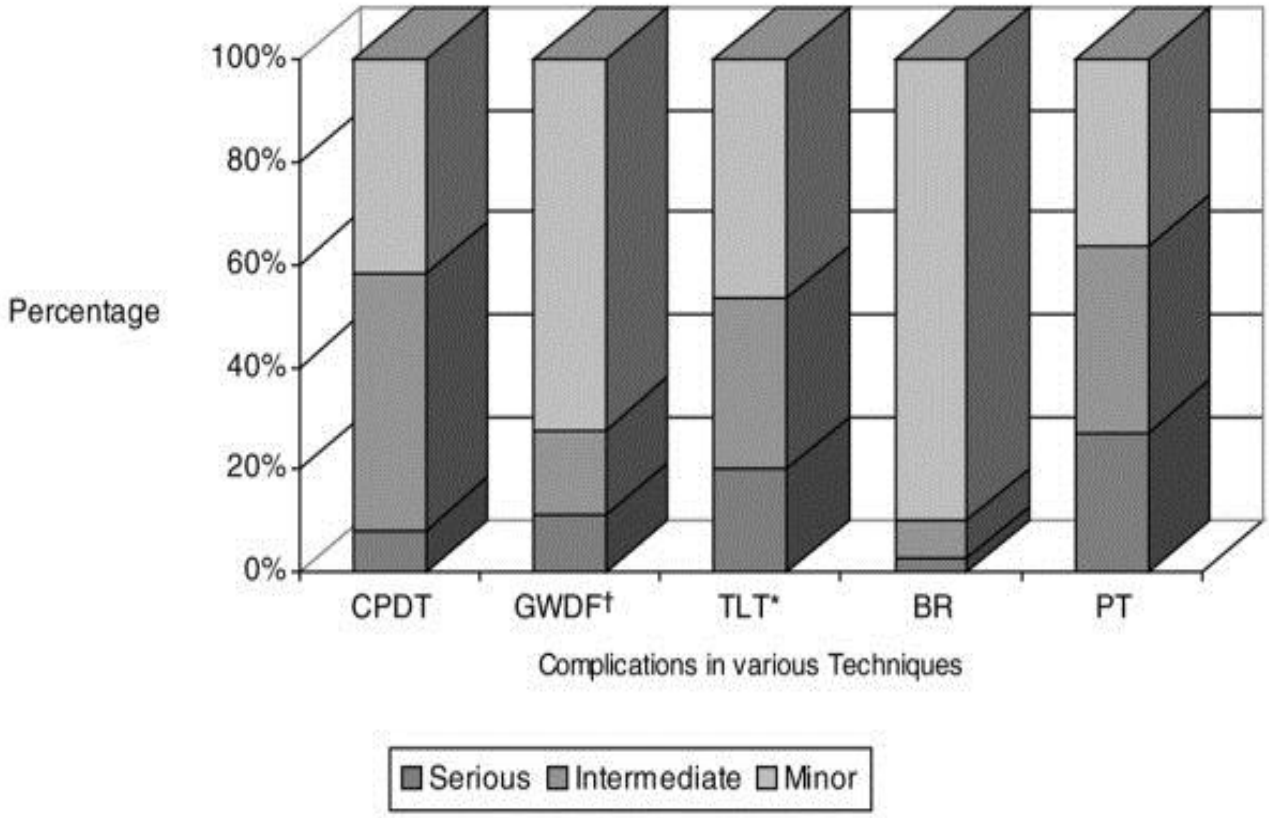
**Rupture of tracheal rings, paratracheal insertion (during the procedure might have led with bronchoscope procedure) (3)

***Hypotension (defined as drop of >30% >5 min)

****Hypoxemia SAO2<90%.

In a comprehensive study of peri-operative complications from the various dilatational percutaneous tracheostomy techniques, Byhahn et al. [5] reported a 23% overall occurrence of complications, with a minimum of 6% for the Ciaglia Blue Rhino® (Cook Medical, Limerick, Ireland) dilator technique. A comparative study of perioperative complications of five PDT techniques, performed by the same team over a 5-year period, is reported in Table 2. Peri-operative complications most frequently associated with dilatational percutaneous tracheostomy techniques include hypotension, hypoxia, bleeding, resistance to the insertion of the cannula, peritracheal tube insertion (with false passage formation), damage to the posterior tracheal wall and fracture of tracheal rings (the latter accounting for about 25% of all complications) [5, 6].

Table 2



A comparison of perioperative complications with five different PDT techniques. *$P < 0.05$ versus any other technique; †$P < 0.05$ versus PDT, TLT and BR. BR, Blue Rhino; CPDT, Ciaglia's percutaneous dilatational tracheostomy; GWDF, guide wire dilating forceps; TLT, translaryngeal tracheostomy; PDT, percutaneous dilatational tracheostomy; PT, Percu Twist technique. From ref.18.

It is often believed that when performing dilatational percutaneous tracheostomies, tracheal rings are displaced, but remain intact. However, a study on cadaveric specimens has shown substantial peristomal mucosal tears and cartilaginous fractures that may lead to clinically relevant tracheal stenosis [22]. The fracture of tracheal rings may be due to the longitudinal force applied during the dilatation phase of the manoeuvre. One study reports the complication of tracheal ring fractures in 9.5% of cases when using the Ciaglia single dilator technique, the latter being generally considered

the safest (and hence the most widely used) among the dilatational percutaneous tracheostomy techniques [3]. A more recent device for dilatational percutaneous tracheostomy utilises a balloon dilation technique imparting a radial force (Ciaglia Blue Dolphin technique). However, this innovative feature was recently questioned by Cianchi et al. [7] who demonstrated the superiority of the Ciaglia single dilator technique(Tracheal ring injury : Rhino group (5.7%), Dolphin group (8.6%), ring buckling : Rhino group (2.9%), Dolphin group (8.6%))

To further improve the safety of percutaneous tracheostomy procedures, we developed a novel dilatational device (the G-Trach), the innovative characteristic of which is a balloon dilator shaped as an inverted cone, with the distal diameter being larger than the proximal diameter (Fig. 1).

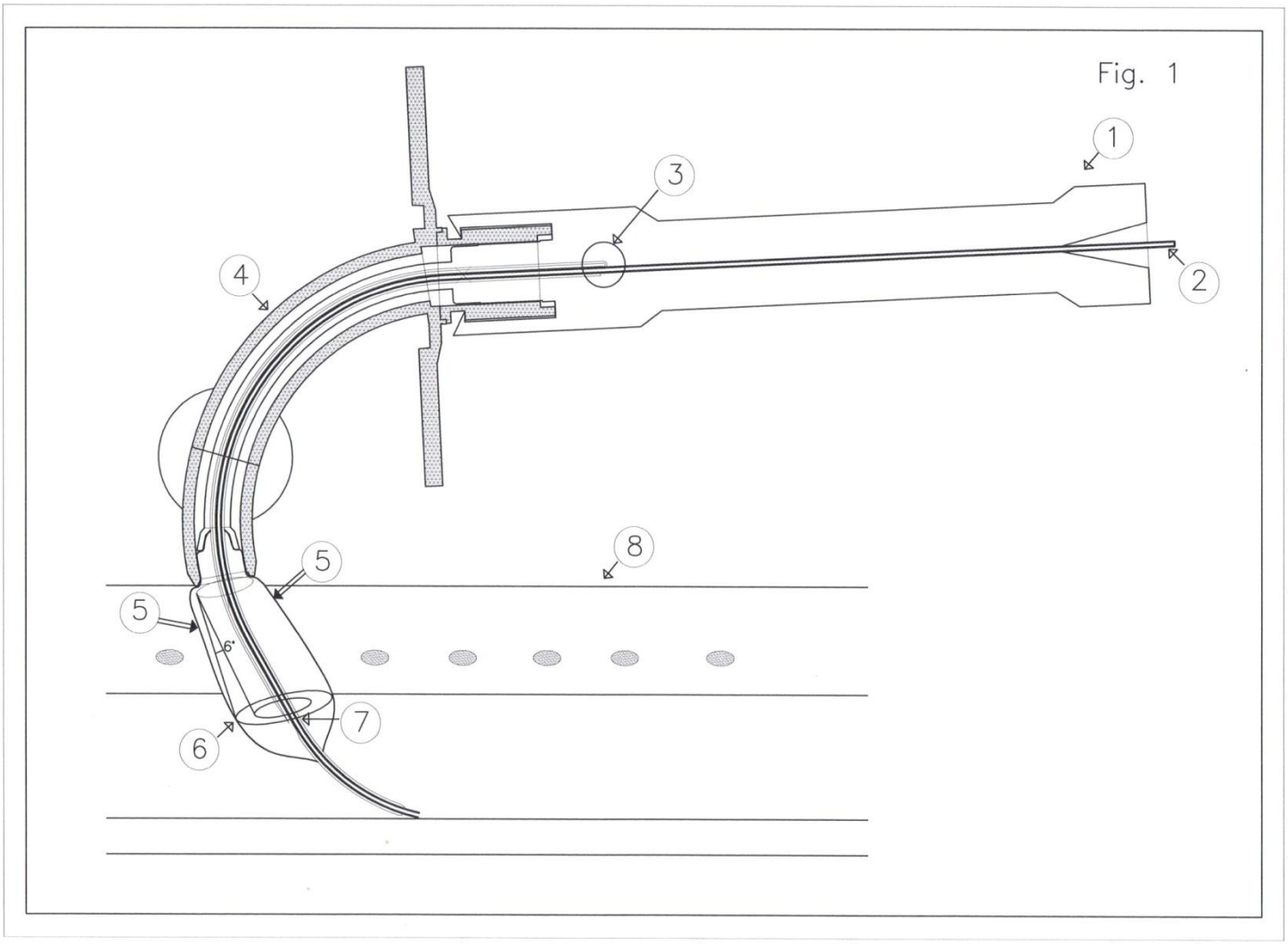


Fig. 1. Longitudinal annotation of the G-Trach device. Note the inverted cone shape of the dilator balloon (6) with its proximal part partially inside (1–2 cm) the tracheal tube. The device incorporates the handle (1), the wire guide (2), and the inflating tube that ends in the distal part of the balloon (3 & 7). The tracheal tube (4), the guide-wire (2) and the skin surface (8) are also represented.

The device uses a G-Trach balloon dilator (made in PET, polymer), the main technical improvements of which are reported below.

1) The balloon dilator in addition to producing a force that expands radially, thus opening a gap between the first tracheal rings, thanks to its special shape facilitates the introduction of the cannula;
2) The inflated balloon in addition to its function as a dilator acts also as a spindle introducer for the tracheostomy tube; in addition, it opens the stoma while compressing the tissues, thus reducing the risk of trauma and bleeding.
3) The procedure is performed in three steps (i.e. one step less than for the other PDT devices): positioning of the deflated balloon (2-4 tracheal rings), inflation of the balloon and subsequent stoma dilation, introduction of the tracheostomy tube.
4) The system is designed to facilitate handling during dilation and introduction of the cannula into the trachea.
Due to these characteristics, the G-Trach is theoretically less harmful to the tracheal rings than the other methods currently employed when performing dilatational percutaneous tracheostomies; it could, therefore, reduce the number of complications associated with the procedure.
To test the safety of the G-Trach device, as well as its practical utilisation, we performed two experimental studies. The first, which was conducted on animals (pigs), showed that the G-Trach was indeed safe and easy to use. We therefore moved to a preliminary study on humans, which is still underway.
The aim of this thesis is to describe in some detail the experimental study on pigs and to describe the study planned on humans, as well as to report the preliminary results obtained so far.

Preliminary study in pigs (see annex 1)

Methods

The study was carried out on eight adult pigs (20–40 kg body mass) at the Veterinary Institute of the Autonomous University of Barcelona in accordance with the institutional guidelines on animal welfare. The protocol was approved by the University's Institutional Review Board.

As mentioned above, the G-Trach is characterised by an inverted cone-shaped dilator balloon that is inflated by means of a tube ending in the distal part of the dilator balloon (Fig. 1). During inflation

this shape facilitates the progression of the balloon along the tracheal tissues. In addition, the inflation of the distal part opens the tracheal rings from inside by compressing the tissue against the tracheostomy tube. The G-Trach allows for a genuinely single-step procedure: the tracheostomy tube, which is firmly attached to the proximal part of the balloon and to the handle, is introduced with the G-Trach apparatus by the operator once the balloon dilator has been inflated (Fig. 2).

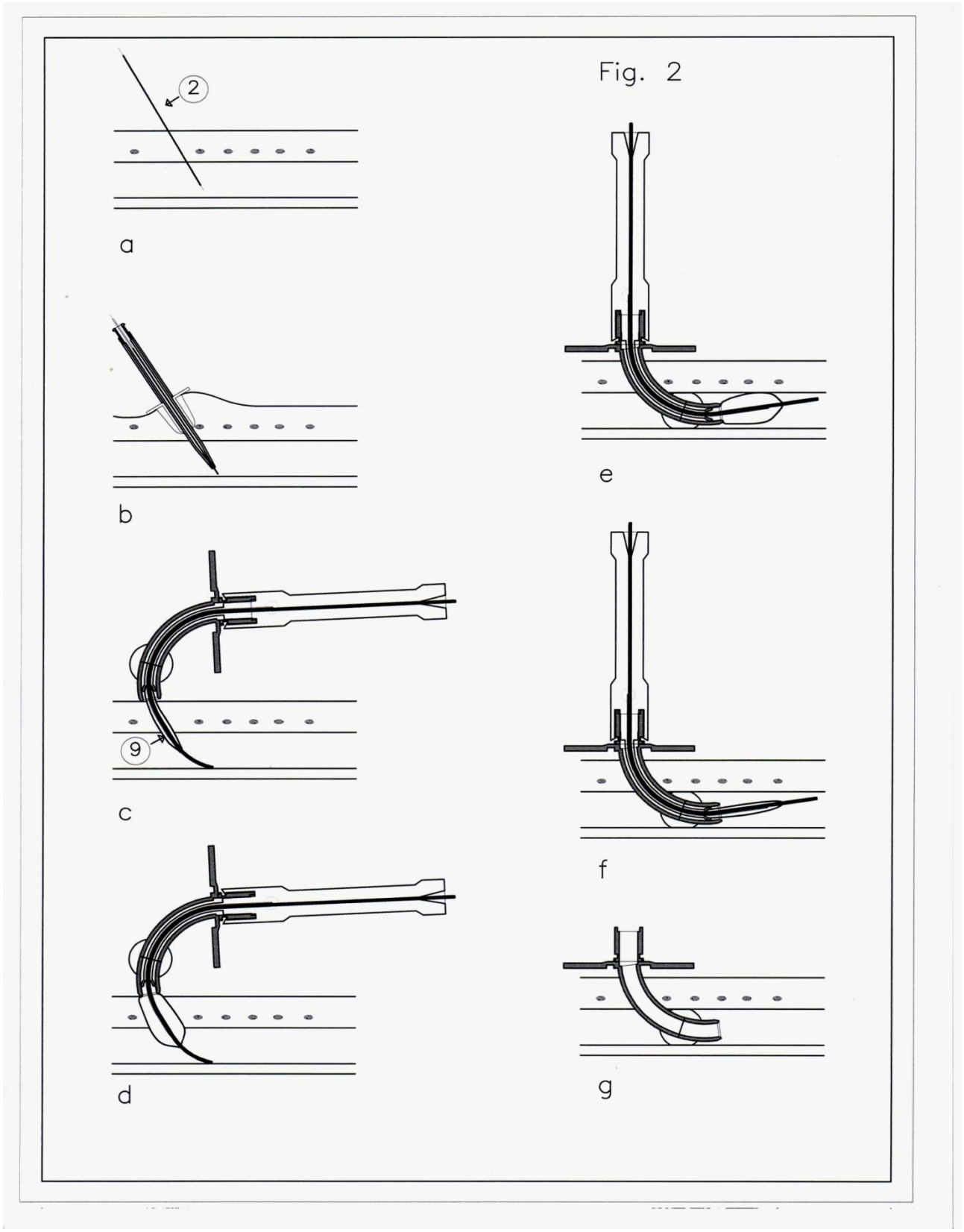


Fig. 2
2
a
b
9
c
d
e
f
g

Fig. 2. The sequence for G-Trach insertion: a: After puncture of the anterior tracheal wall by a needle, the guide-wire is inserted through the needle bore (2); b: Insertion of the small dilator over the guide-wire; c: Introduction of the G-Trach apparatus along the guide-wire across the tracheal wall with the tracheostomy tube hooked to the handle. The deflated balloon is introduced through the anterior tracheal wall (9); d: Balloon inflation. The expansion forces during inflation (7–10 atmospheres) facilitates introduction of the tube into the trachea; e: After dilation of the tracheal wall, the tracheostomy tube is inserted into the trachea. The dilator tube is still inflated and used as an insertion device; f & g: After balloon deflation, the G-Trach apparatus is removed leaving the tracheostomy tube in the trachea.

The animals received premedication with intramuscular morphine 0.4 mg.kg−1, ketamine 10 mg.kg−1 and azaperone 4 mg.kg−1. Anaesthesia was induced using 10 mg.kg−1 of intravenous thiopental, following which the animals underwent tracheal intubation. Anaesthesia was maintained using inhaled isoflurane at 2%. Heart rate, blood pressure and arterial blood oxygen saturation were monitored by catheterisation of the femoral artery. After evaluation of the anatomic aspects of the throat and an injection of lidocaine 1%, a 17-G cannula was inserted between the first tracheal rings. In the four largest pigs (40 kg) in whom the distance between the skin and the trachea was greater than 4 cm, needle placement was preceded by an engraving of the rind to achieve a depth to the trachea of 3.5–4.0 cm compatible with the length (5.0 cm) of the dilator balloon of the G-Trach device. A needle was used to estimate the correct engraving depth. A guide wire of 0.38 mm diameter was then positioned through the needle into the trachea (Fig. 2a). In the other four pigs, a longitudinal 3-cm incision of the skin was performed with a scalpel and was followed by insertion over the guide wire of a 14-F dilator to facilitate the insertion of the deflated balloon (Fig. 2b). A large amount of lubricant was used before insertion of the balloon and the cannula. The dilator balloon of the G-Trach, loaded with a tracheostomy tube of 8.5 mm internal diameter (Rusch Tracheofix™, Teleflex Medical, Varedo, Italy), was then introduced into the trachea and inflated with 15–20 ml saline 0.9% to a pressure of 7–10 atmospheres using a locking syringe equipped with a pressure gauge (Figs 2c & 2d). After inflation only a little force was exerted on the handle to allow the introduction of the cannula (Fig. 2e). Once the tracheostomy tube was positioned, the balloon was immediately deflated and removed leaving the tracheostomy tube in place (Figs 2f & 2g).

A photograph of the equipment used is shown in Fig. 3.

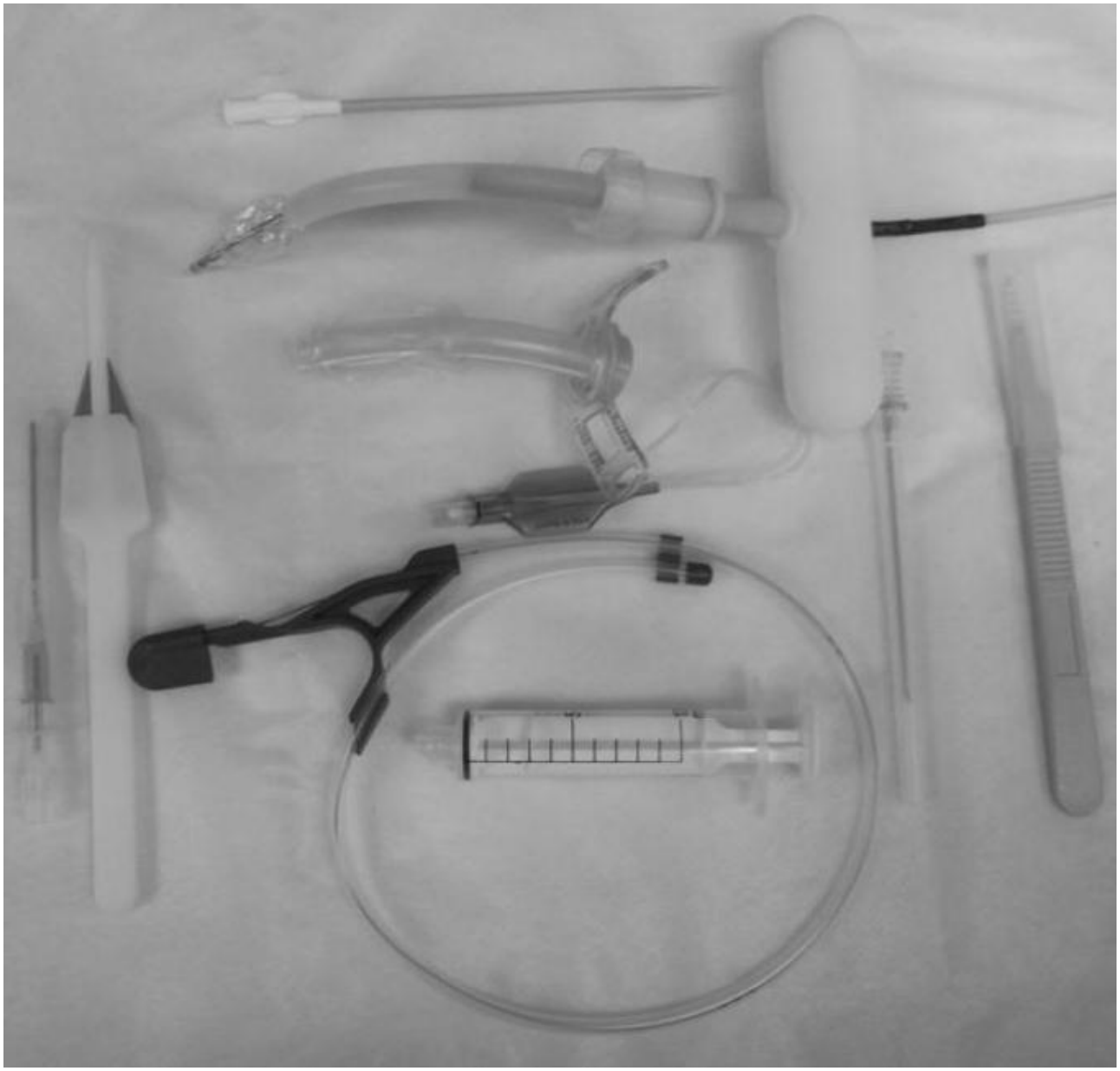


Fig.3

After removal of the or tracheal tube, the pigs' lungs were ventilated for 5–10 min via the tracheostomy tube. Following this they were euthanised and their tracheas opened to evaluate the correct position of the cannula, the presence of any posterior wall tracheal injuries, and any broken tracheal rings. The size of the trachea was also measured by means of a feeler gauge.

Preliminary study in pigs - Results

The mean (SD) time from tracheal puncture to ventilation through the tracheostomy tube was 2.63 (0.64) min. The mean (SD) time for inflating the balloon, dilating the subcutaneous and tracheal tissues, and introducing the cannula was 0.71 (0.38) min. There was no visible bleeding from the tracheostomy site, either externally or into the trachea. The post-tracheostomy ventilation and post-mortem evaluations confirmed correct positioning of the cannula. Neither injuries to tracheal rings and posterior trachea wall, nor occult bleeding were detected at post-mortem trachea examination. In all the eight pigs, heart rate, rhythm, blood pressure and arterial oxygen saturation did not change significantly during the procedure (Table 2). The internal diameter of the pigs' trachea ranged from 12 to 15 mm.

Table 2. Heart rate, blood pressure and arterial oxygen saturation measured in 8 pigs before (baseline) and during the procedure. Values are mean (SD).

MAP, mean arterial pressure; SaO2, arterial oxygen saturation.			
Heart Rate (bpm)	88.2 (8.1)	92.8 (11.7)	0.121
MAP (mmHg)	69.0 (4.5)	73.2 (6.2)	0.081
SaO2 (%)	97.0 (1.1)	95.8 (3.2)	0.108

Study in humans

The positive results derived from the study on pigs, lead us to design an “exploratory pilot” study to test the G-Trach device (CE brand with the CE code 0120) for tracheotomy percutaneous dilated (PDT) in humans with the aim of evaluating the efficacy and safety of the device. Indeed, CE marking of medical devices allows them to be commercialized and utilised within the European Union.

Therefore, and before embarking in complete study in humans while waiting for clearance of the responsible the Ethics Committee (see Annex), data were collected in six cases of tracheostomy performed with the G-Trach. The aim of this preliminary survey was that of defining I) any eventual possible corrections of the product, the build quality of the device and of the equipment set and of allowing ii) the learning procedures for the operators.

Annex - Prospective study design in humans

The prospective study on the safety and efficacy of the G-Trash device for tracheostomy, is expected to enroll 42 patients of ICU receiving mechanical ventilation for a prolonged period (expected> 14 days). These patients will be selected among those admitted to the ICU of the Emergency Department (Azienda Ospedaliero-Universitaria Santa Maria della Misericordia - Udine) and receiving mechanical ventilation for a prolonged period with an indication for percutaneous dilatational tracheostomy (PDT).

Inclusion criteria: Patients with oro-tracheal intubation in mechanical ventilation expected duration of 14 days or more, over the age of 18 years.

Exclusion criteria: emergency response, pre-existing infections or malignancies of the site for tracheotomy, with fracture of the cervical spine instability or uncontrolled intracranial hypertension; hypertrophy of the thyroid; presence of coagulopathies or anticoagulant therapy with INR value> 1.5; severe thrombocytopenia with platelet counts $<50.000mm^{-3}$.

The data to be collected will include: type of patient; physiological parameters during the intervention; time between tracheal puncture and placement of the tracheal tube; difficulties in insertion of the tracheal tube requiring more than one attempt. Furthermore, the data collection will include procedure-related complications as unusual bleeding; tracheal ring injury; hypoxia (defined as a pulse-oximetry oxygen saturation below 90%); pneumothorax, as well as post-operative data such as presence of unusual bleeding of tracheal mucosa or cutaneous bleeding 6 h after

procedure. The data collection will be prospective. The Azienda Ospedaliero Universitaria of Udine will be the coordinating center for the collection of data.

Safety end-points: peri-operative study.

-Major complications (specific to the procedure): esophageal perforation; tracheal laceration; tracheoesophageal fistula (confirmed by bronchoscopy during and after the procedure); estimated Major bleeding: > 100ml.

Major complications (non- specific): cardiopulmonary arrest.

- Complications of intermediate gravity (specific): breaking of tracheal rings, paratracheal insertion (confirmed by bronchoscopy during and after the procedure); resistance to the cannula (difficulties in insertion of the tracheal tube requiring more than one attempt or stop of the procedure).

Complications of intermediate severity (non-specific): Respiratory arrest (> 5 min); hypotension (defined as a decrease of > 30% and > 5 min); estimated Minor bleeding: > 25 < 100 ml.

- Minor complications (specific): bleeding surface estimated < 25 ml, puncture of the cuff of the endotracheal tube.

Minor complications (non-specific); loss of airway < 5min; hypoxemia SaO2 <90%.

The time necessary for the recruitment of patients, given the type of intensive therapy, is estimated in about 12 months.

Tracheostomy procedure will be carried out under direct fibreoptic bronchoscopic video guidance. General anaesthesia will be induced using propofol, midazolam and fentanyl for analgesia, followed by a continuous infusion of propofol; neuromuscular block will be used used if necessary. Arterial pressure will be controlled. Inspiratory fraction of oxygen will be set between 0.5 and 1.0 as required. Physiological parameters and expiratory CO2 will be monitored continuously.

Asepsis will be assured with chlorhexidine 2% and lidocaine 2% infiltrated locally. Fibreoptic video guidance will allow the control of the correct position of needle insertion (between the second-third tracheal ring) and prevent unintentional punctures of the posterior tracheal wall. The sequence of the tracheostomy procedure is explained in fig.2.

Study Design: safety and efficacy of the G-Trach Tracheotomy.

Success rate is defined as the absence of major complications (tracheal laceration, esophageal perforation, bleeding > 100 ml, cardiopulmonary arrest).Data collection: prospective. - Sample size: 42 patients calculated for endpoint security. - Sample size was based on the optimal two-stage Simon design, i.e. the study will be interrupted at the end of the first phase (19 patients) if the security will turns out to be inadequate (success observed in less than 17 patients). If ≥ 17 successes will be observed in the first 19 patients, the study will be extended to a total of 42 patients (23 new patients to be enrolled in phase 2). At the end of the study, if ≥ 38 successes are observed, the (null) hypothesis (i.e. the

probability that the true success is ≤ 80%) will be rejected and further investigation of G-Trach tracheotomy device in this patient population is warranted.

Retrospective study in humans – Results

As mentioned above, before starting the prospective study on the efficacy and safety of the G-Trach, pending the opinion of the ethics committee, six tracheostomies were performed with the device. Indeed, the use of the device G-Trach is authorized by the CE code (number 0120), which guarantees the safety of construction and material compatibility, without ensuring its effectiveness, and allows it to be commercialized and utilised within the European Union. Tracheostomies data were collected in a retrospective study from the medical records of patients, from a data card procedures tracheostomy in the ICU. Impressions and comments of the operator on the advantages, disadvantages and improvable aspects of tracheostomy with G-Trach device, were collected through an interview.

Six patients (5 males and 1 female) admitted to the ICU were submitted a tracheotomy with the G-Trach device (see table3). The patients suffered from head injury stabilized with the exception of a one patient admitted to the hospital of Gorizia, who suffered from severe cerebral bleeding stabilized. These 6 patients were undergoing mechanical ventilation > 14 days. Informed consent was obtained from patients or their relatives if patients were unable to consent before the procedure. According to the procedure the patients were under anaesthesia, monitoring of vital signs and bronchoscopy, during the procedure. The maximum number of attempts for the insertion of the tracheal tube was set at two, after which, the procedure was arrested and replaced by the use of a different device. Indeed, two attempts during the procedure are considered acceptable for patient safety, as described in other scientific studies on PDT devices (7,16).

Tab.3 Procedural data patients retrospective study

Number patients		6
Age (years)		60 (30 - 75)
Body Mass Index (kg/m²)		25 (28-20)
Time from admission to tracheostomy (days)		>14
Duration of procedure (min)		5(2-8)
Resistance to tracheal tube passage with stop procedure.		2

-The two tracheotomies which were interrupted after the second trial were carried out with the Ciaglia Blue Rhino PDT technique

-The duration of the procedure, collected from the folder ICU procedures, is the time (min) elapsed from tracheal puncture to tracheal tube insertion.

- No significant complications were recorded, with minimal bleeding and no changes in vital signs (Mean Systemic Pressure, SaO2. Heart Rate)

-The dilator balloon of the G-Trach, loaded with a tracheostomy tube of 8.5 mm internal diameter (Rusch Tracheofix™, Teleflex Medical, Varedo, Italy), was then introduced into the trachea and inflated with 15–20 ml saline 0.9% to a pressure of 7–10 atmospheres using a locking syringe equipped with a pressure gauge

In two cases the dilated phase was repeated two times, extending the time required for the progression of the tube into the trachea to 7 - 8 min. The tracheal tube insertions requiring more than one attempt is reported to be 5.7% for Ciaglia Blue Rhino and 28.6% for the Ciaglia Blue Dolphin Percutaneous Tracheostomy, by G.Chianchi and coll. (7,16)

Two cases have been suspended after the second attempt, in which cases the tracheostomy was concluded with the Ciaglia Blue Rhino PDT technique

The comments collected in an interview operators were:

Advantages:

- The procedure was more effective (than the other PDT procedures) in two cases, equally effective in the other two cases.

- The procedure requires one step less than the other PDT procedures.

- The time required for the dilation and introduction of the tracheotomy tube was on the order of 5 minutes.

- Bleeding was comparable with other PDTs.

- Minimal changes in vital signs (Mean Systemic Pressure, SaO2. Heart Rate) were observed.

- The thrust generated by the inverted cone-shaped balloon during inflation was such that the progression balloon in the trachea could not be stopped.

Disadvantages:

- Skin incision of 15-20mm, comparable with other techniques.

- Risk of skin capture between the distal balloon dilator and tracheotomy tube, thus preventing the progression into the trachea.

- The need to provide a continuity in the transition between the balloon dilator and the tracheostomy tube during the progression into the trachea.

Discussion

The complications associated with dilatational percutaneous tracheostomy procedures are, without doubt, fewer than those associated with the traditional surgical tracheostomy technique [9]. Nevertheless, significant complications are still reported with the use of the various commercially available devices for dilatational percutaneous tracheostomy [5]. Rupture of the tracheal rings and injury to the posterior wall of the trachea are the most frequent and dangerous complications described [22,3]. These complications are partially due to the downward and longitudinal forces applied to the surrounding tissues and posterior tracheal wall during the dilation phase of the Ciaglia single dilator technique. Conversely, the G-Trach dilator balloon system applies a radial force to the peritracheal structures that ought to dilate the tracheal rings without tearing or damage. Moreover, the absence of downward force associated with the use of the balloon dilator system reduces the risk for posterior wall injuries. The same advantages have been postulated for a dilatational percutaneous tracheostomy device using the balloon technique for dilation (Blue Dolphin, Cook) [22]. The G-Trach differs from this latter device in the shape of its balloon a fact that we believe introduces a major technical improvements. The inverted-cone shape of our device facilitates a quick introduction of the cannula into the trachea after inflation of the dilator balloon. In the preliminary study on pigs, the mean (SD) time required for the introduction of the cannula was 0.71 (0.38) min), a substantial shortening of the overall time normally required for the procedure, thus reducing the risk of hypoxia. In addition, since the dilation was followed by insertion of the tracheal tube without interruption, the peritracheal tissues were kept constantly under pressure with a reduced risk of bleeding.

Pigs were used to test this technique because the anatomy and size of pig tracheas are similar to those in humans. Based on our experience, the average depth from the skin to the trachea is about 1–2.5 cm in ICU patients. In our pigs, the depth between the skin and the trachea varied from 3 to 6 cm. This, together with the greater tracheal collapsibility in pigs, makes the procedure somewhat complicated in these animals; we therefore expect a higher probability of success in humans.

In conclusion, this first experience in eight pigs showed that G-Trach system can be used safely for the placement of a tracheostomy tube. Moreover, the G-Trach appears to be easy and quick to use, and offers potential advantages compared with the methods currently used for dilatational percutaneous tracheostomy.

The first six tracheostomies with G-Trach device in humans have partly confirmed the indications

of the studies in pigs. The device has proved easy to use and the three steps procedure immediately intuitive and extremely fast in the introductory and dilation stages; in two cases with a time close to 2 minutes. The first phase of the procedure (puncture with the needle, wire introduction, skin neck incision, first dilatation using 14 Fr, introduction of the deflated balloon) is somewhat longer (2-3min). In two cases the dilated phase was repeated two times, extending the time required for the progression of the tube into the trachea to 7 - 8 min. The tracheal tube insertions requiring more than one attempt is reported to be 5.7% for Ciaglia Blue Rhino and 28.6% for the Ciaglia Blue Dolphin Percutaneous Tracheostomy, by G. Chianchi and coll. (7).
Two cases have been arrested after the second attempt, as required by the Protocol, in which cases the procedure was concluded with the Ciaglia Blue Rhino PDT technique. In these cases, the obstacle to progression was due to the fact that the skin had been hooked between the distal balloon dilator and the tracheotomy tube.

The first tracheotomy with the G-Trach, carried out at the ICU of the Gorizia Hospital, although showing the effectiveness of the device, evidenced the risk of the capture of the skin between the distal balloon dilator and tracheotomy tube, a risk that was initially overcome with a skin incision larger than predicted. (2-3 cm).
The following five cases of tracheotomy performed at the ICU of Udine were carried out with a new device with a wedge placed inside the dilator balloon.(FIG.4).This modification of the device has been reported, and rectified by the CE Committee prior to its use. The result of this modification is that of widening the base of the deflated balloon near the distal end of the tracheotomy tube, thus displacing the peritracheal tissues, which therefore are not captured by the balloon dilator during the initial inflation phase.

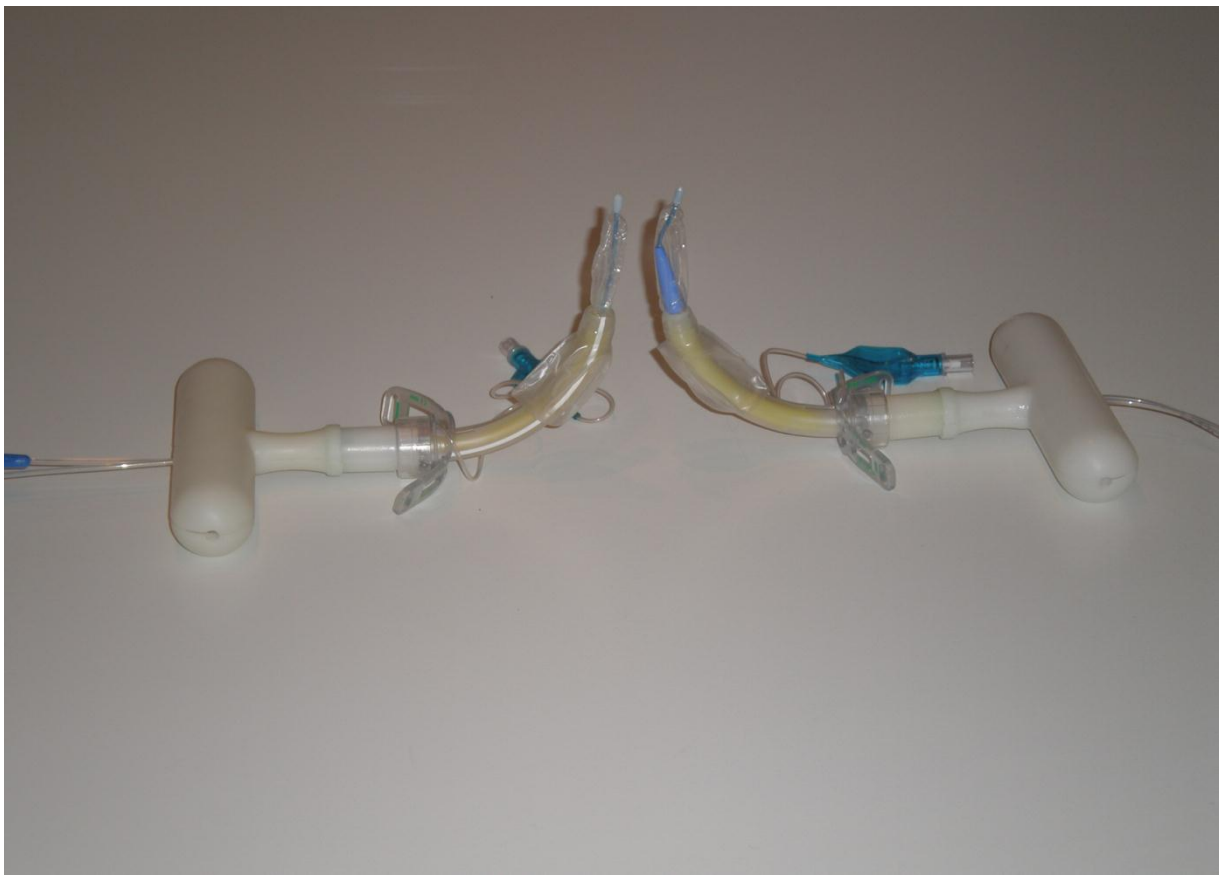
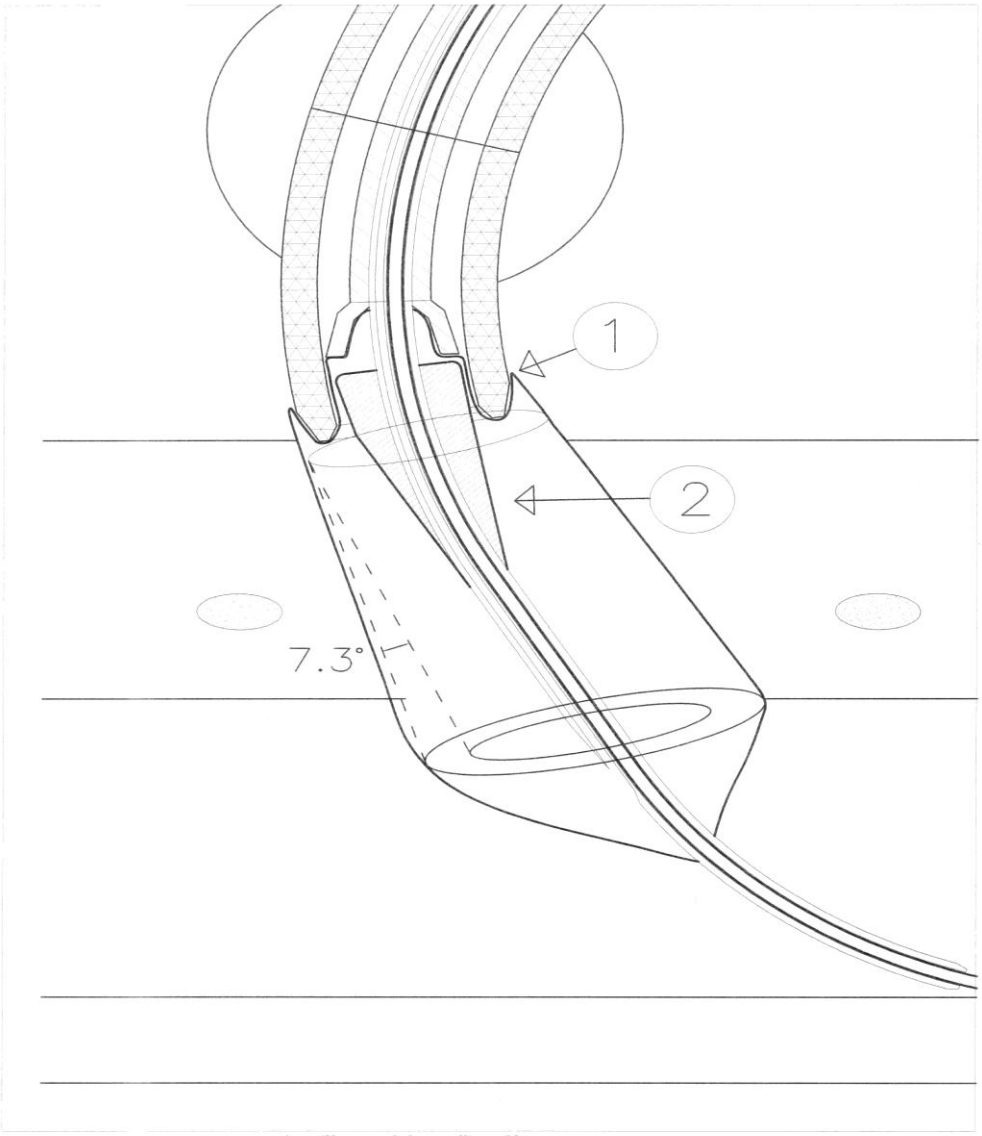


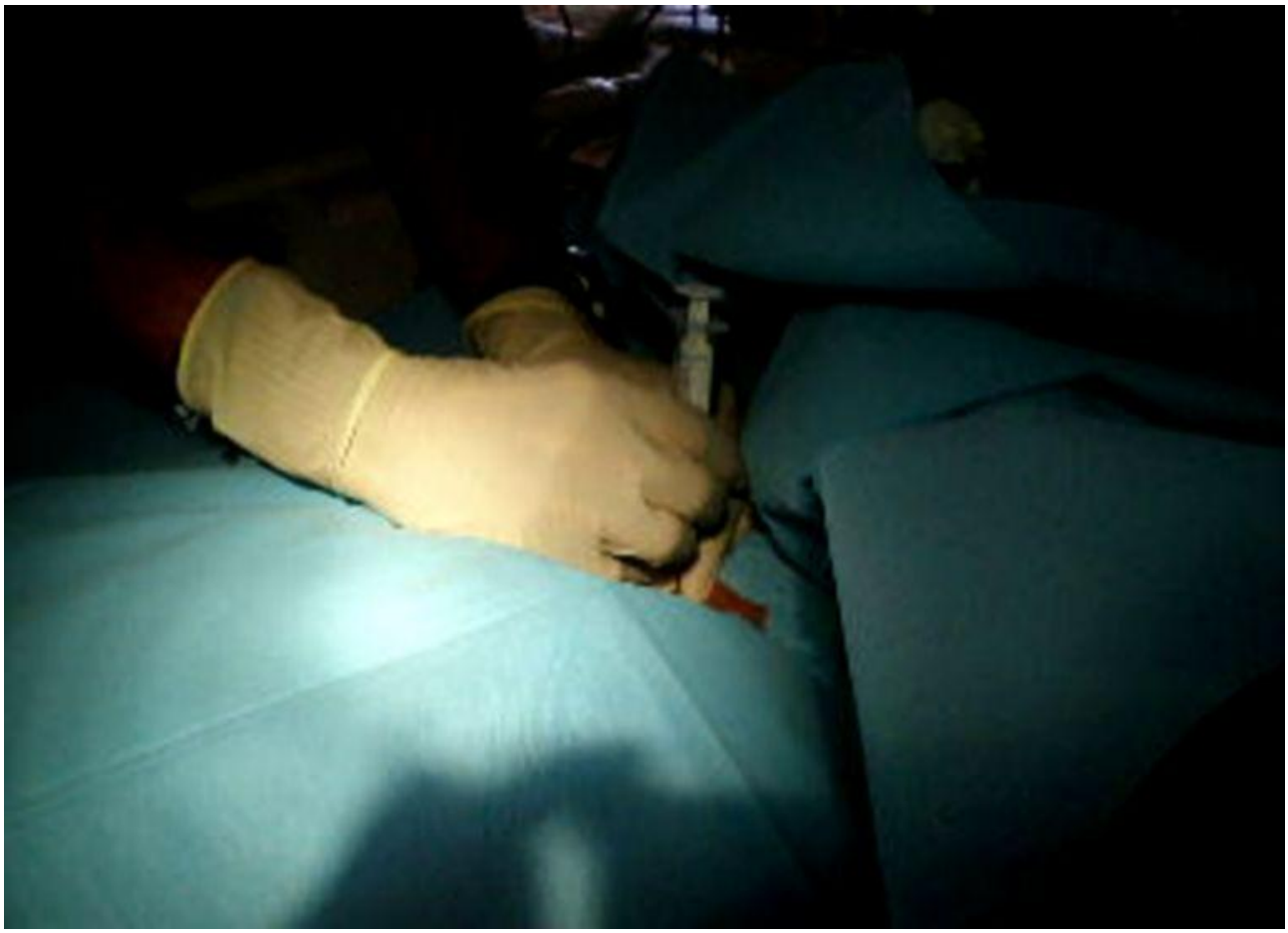
Fig.4 The new device with a wedge placed inside the dilator balloon is shown on the right.

This modified device has proved better than the previous one, but still not up to the level of providing a continuity in the transition between the balloon dilator and the tracheostomy tube during the progression into the trachea, and to reach the desired standard of efficacy.
However, the operators' impression was that actual thrust generated by the balloon during inflation was such that the balloon progression into the trachea could not be arrested. The generation of this thrust was indeed the reason behind the balloon inverted cone shape. Furthermore, if the proximal portion of the balloon wraps the final part of the tracheotomy tube, this thrust will terminate only after the entry of the tip of the tracheal tube into the trachea (Fig.5). In addition, the three steps procedure was very well accepted by the operators who positively judged the fact that the continuity between dilatation and introduction of the device brings about a shortening of the procedure time, thus reducing the risks of bleeding and hypoxia (see photographs' sequence of tracheostomy procedure with G-Trach).

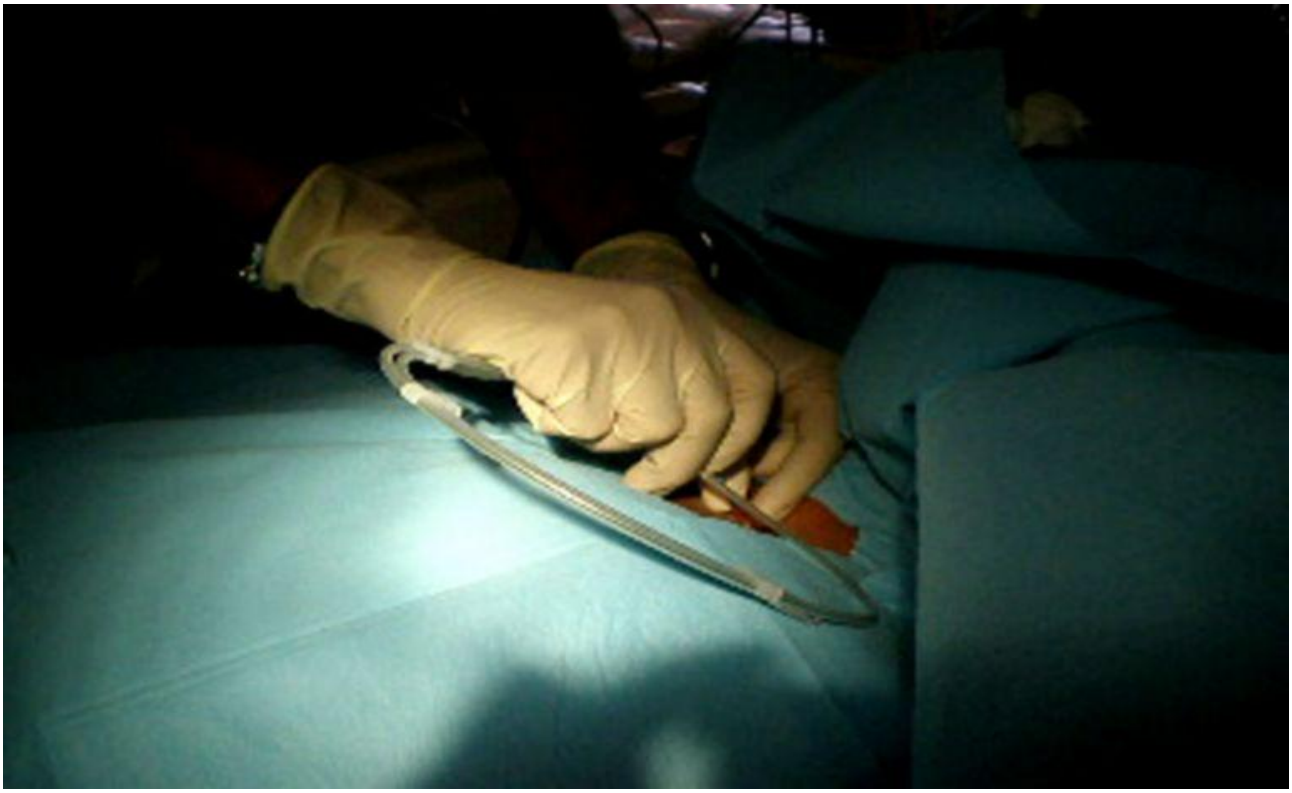
Fig.5 Longitudinal view with the dilating balloon inflated, with the proximal section wrapping on, and projecting beyond, the distal edge of the tracheotomy tube portion (1); the wedge placed inside the dilator balloon (2); the inverted cone shape of the dilator balloon with an angle of 7-8°degrees is also shown.



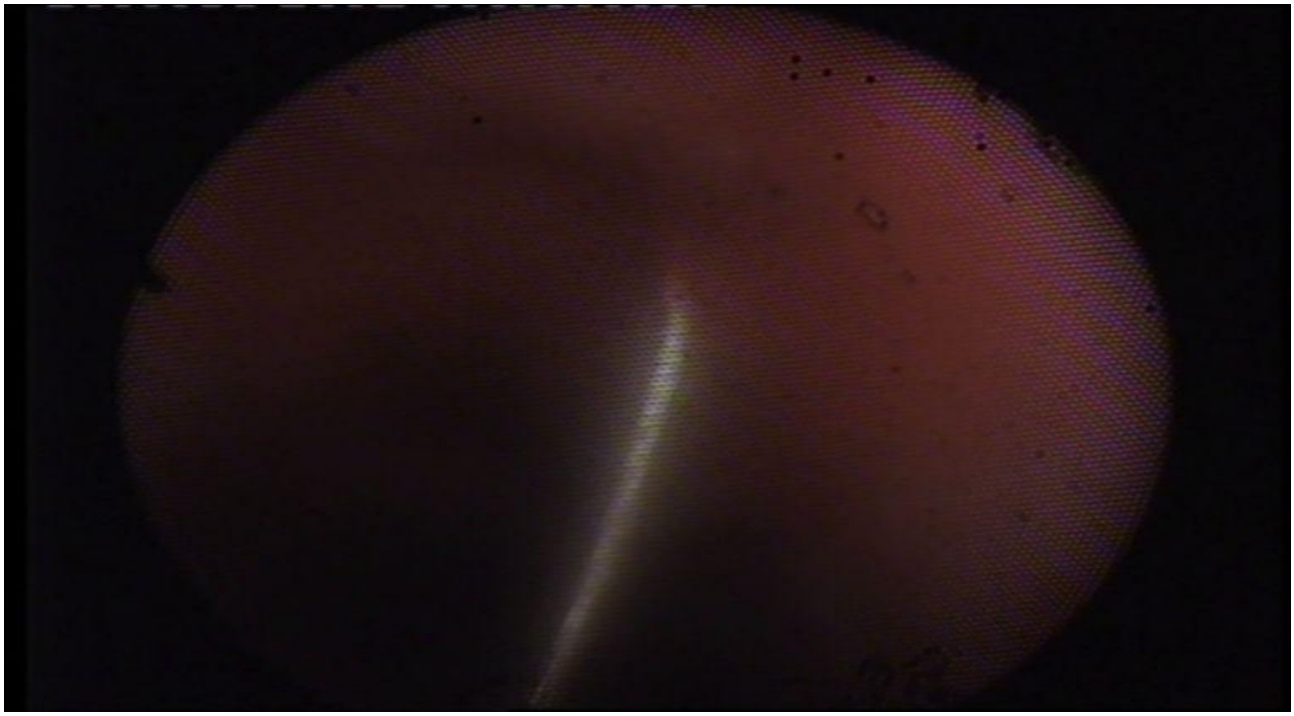
Photographic sequence of the procedure of tracheostomy with G-Trach device.

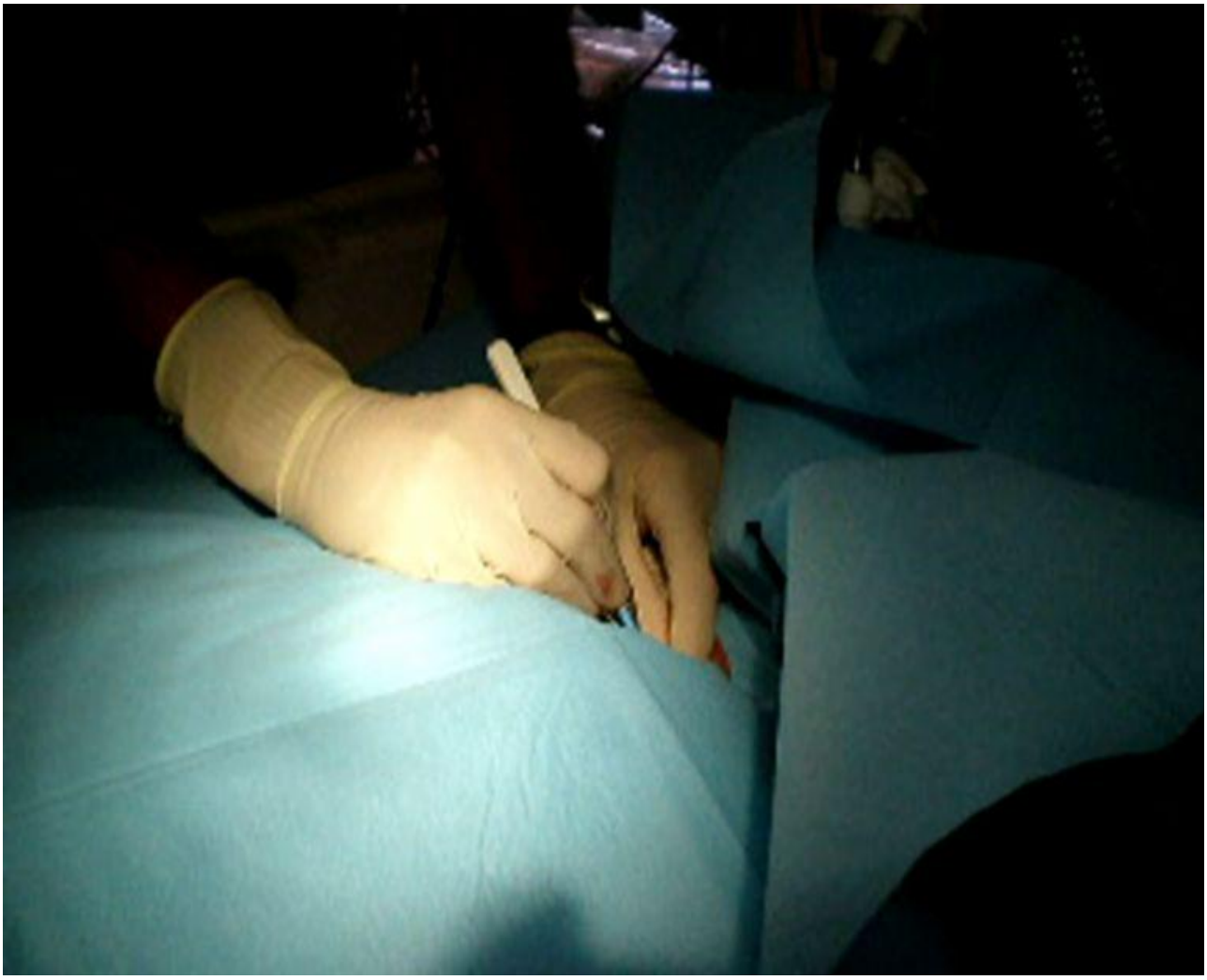


1. Puncture of the anterior tracheal wall with a needle.

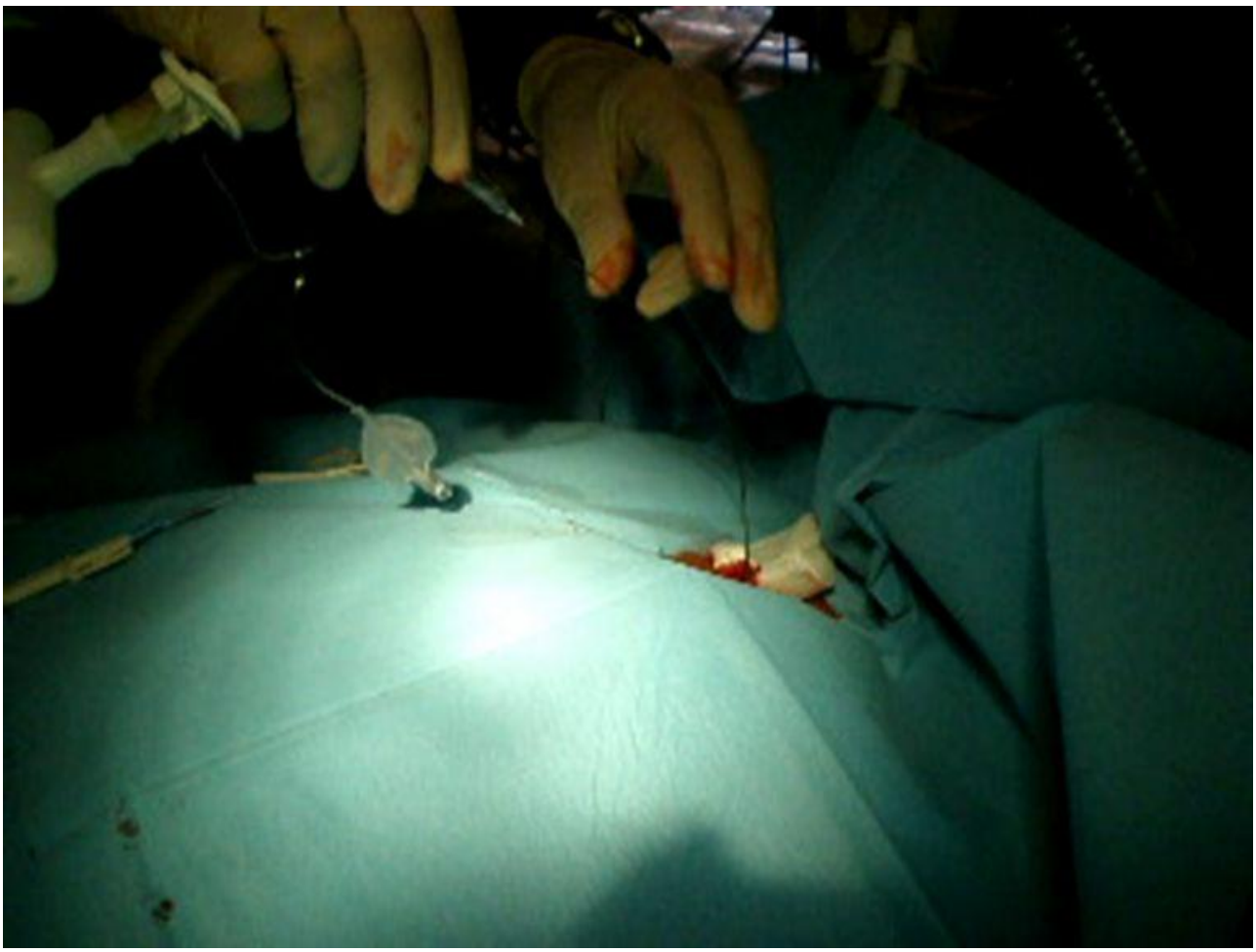


2. The guide wire is inserted through the needle bore, between the second and third tracheal rings. Below, the same procedure observed via the Bronchoscope

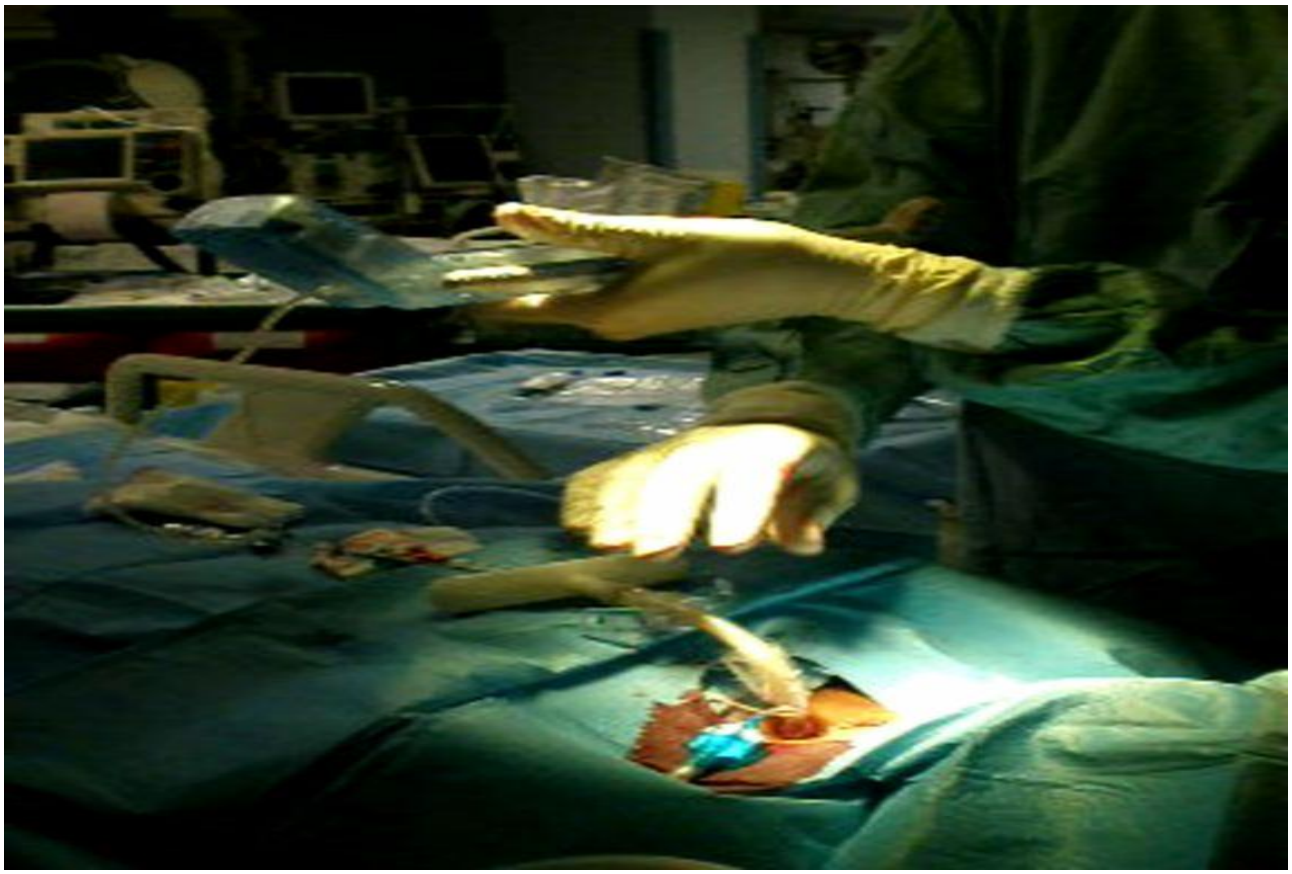




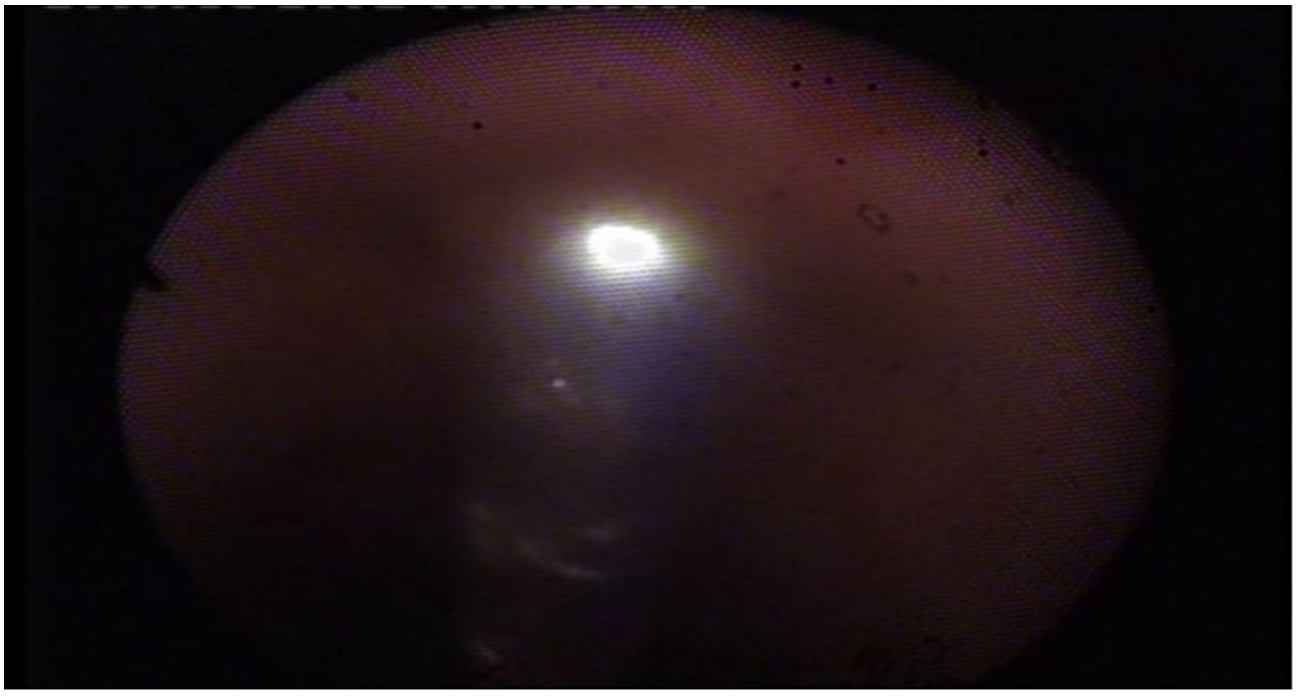
3. Insertion of the small dilator over the guide wire.

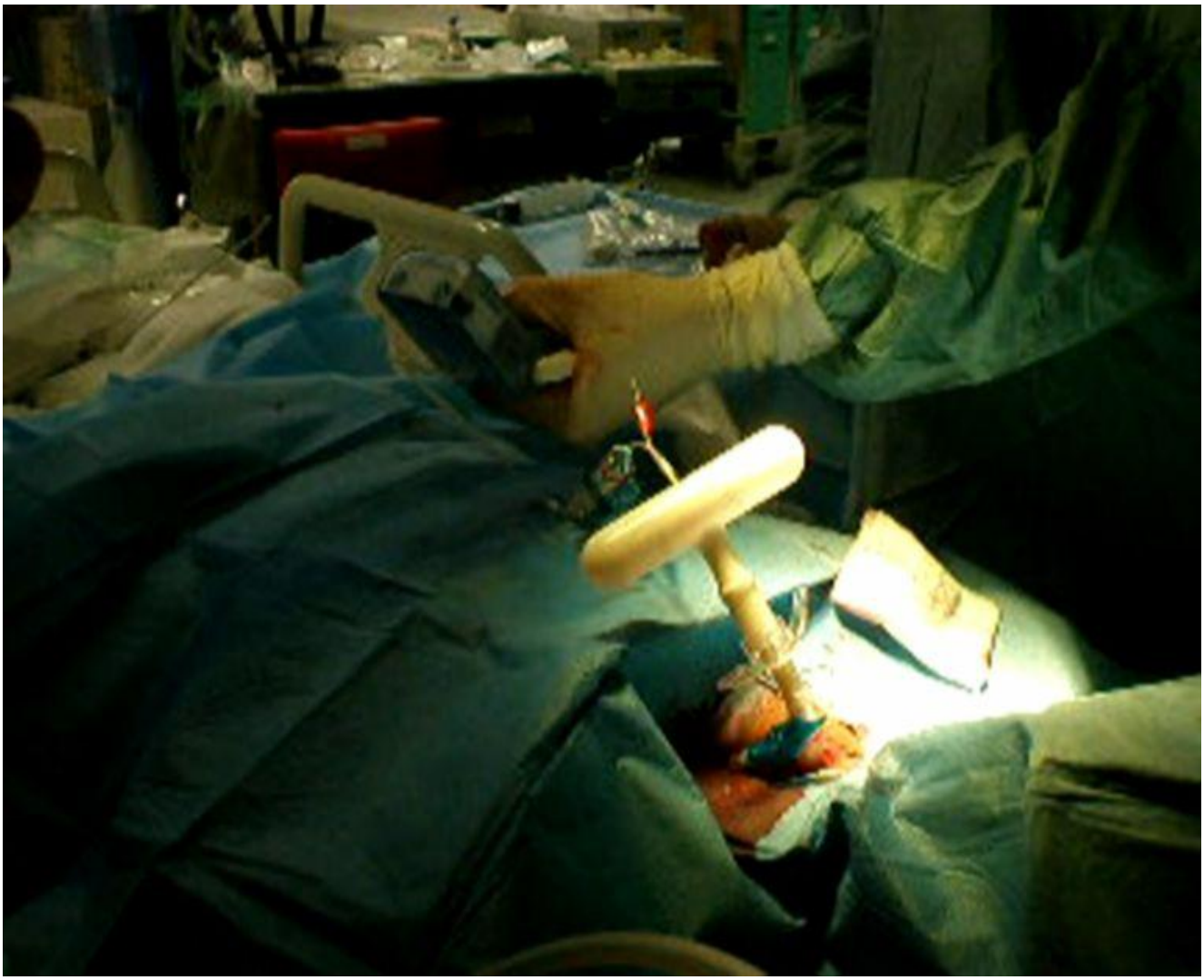


4. Introduction of the G-Trach along the guide-wire across the tracheal wall with the tracheostomy tube hooked to the handle. The deflated balloon is introduced through the anterior tracheal wall.

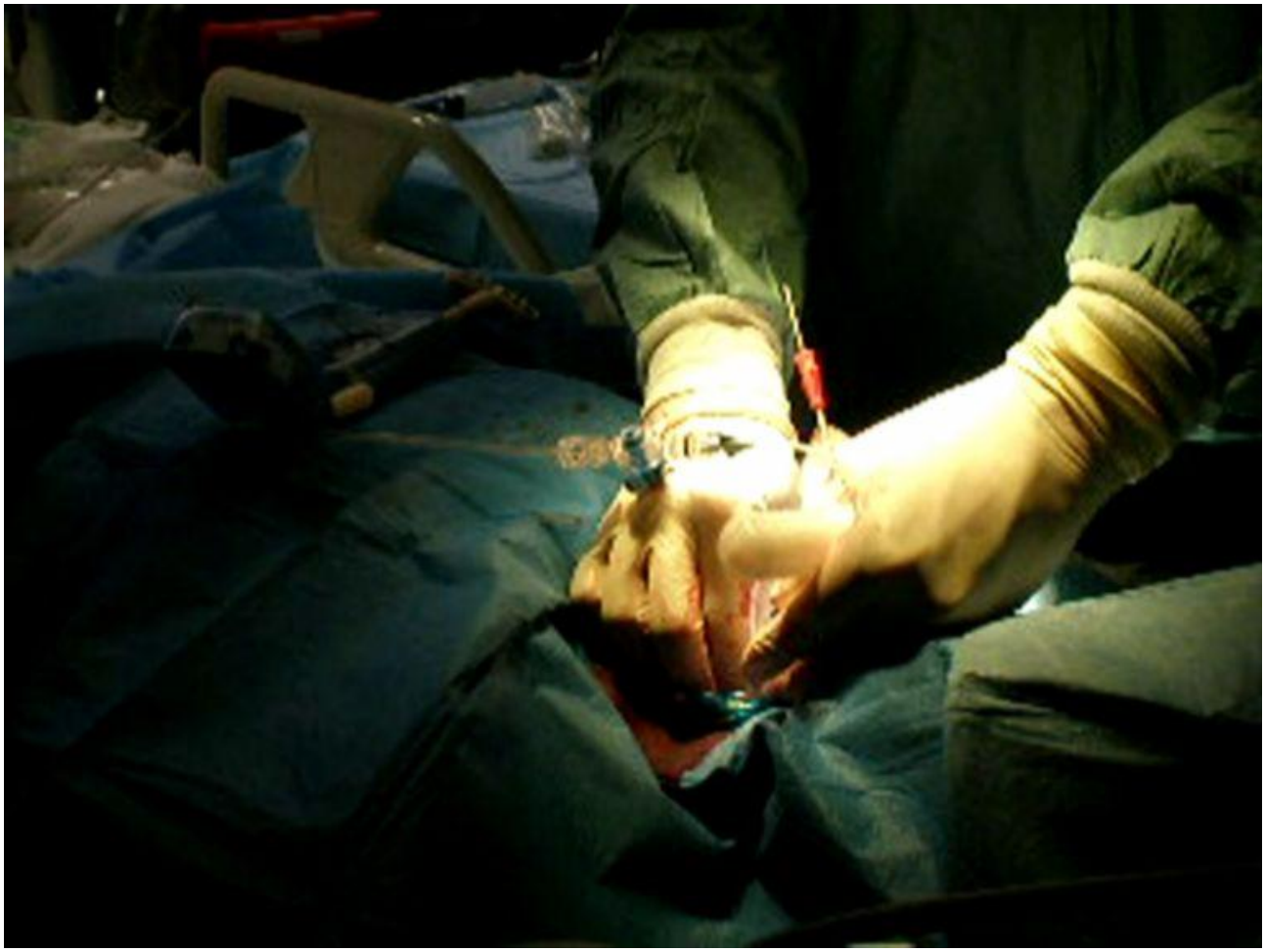


5. Balloon inflation. The expansion force during inflation (7–10 atmospheres) facilitates the introduction of the tube into the trachea. Below, the deflated balloon observed via the Bronchoscope.

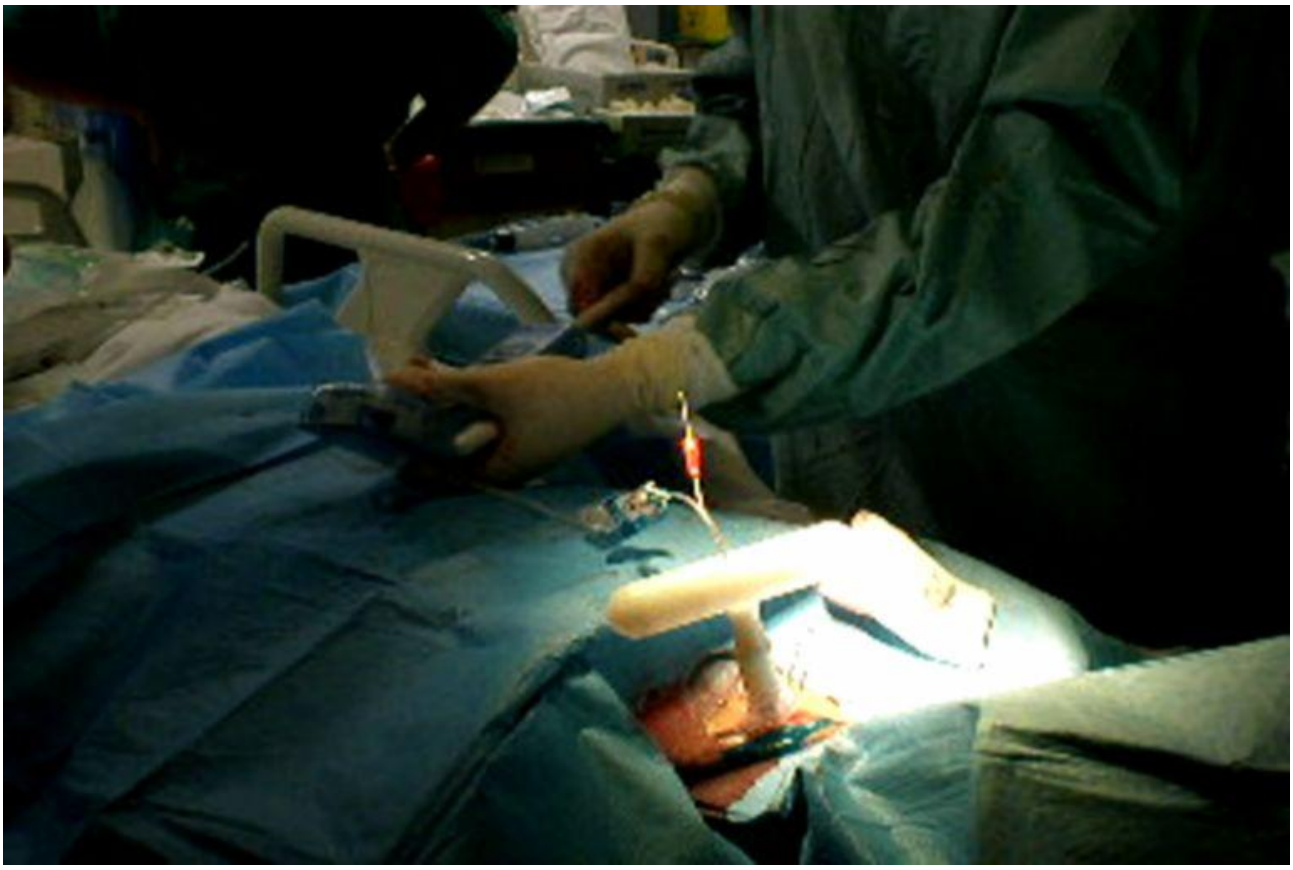




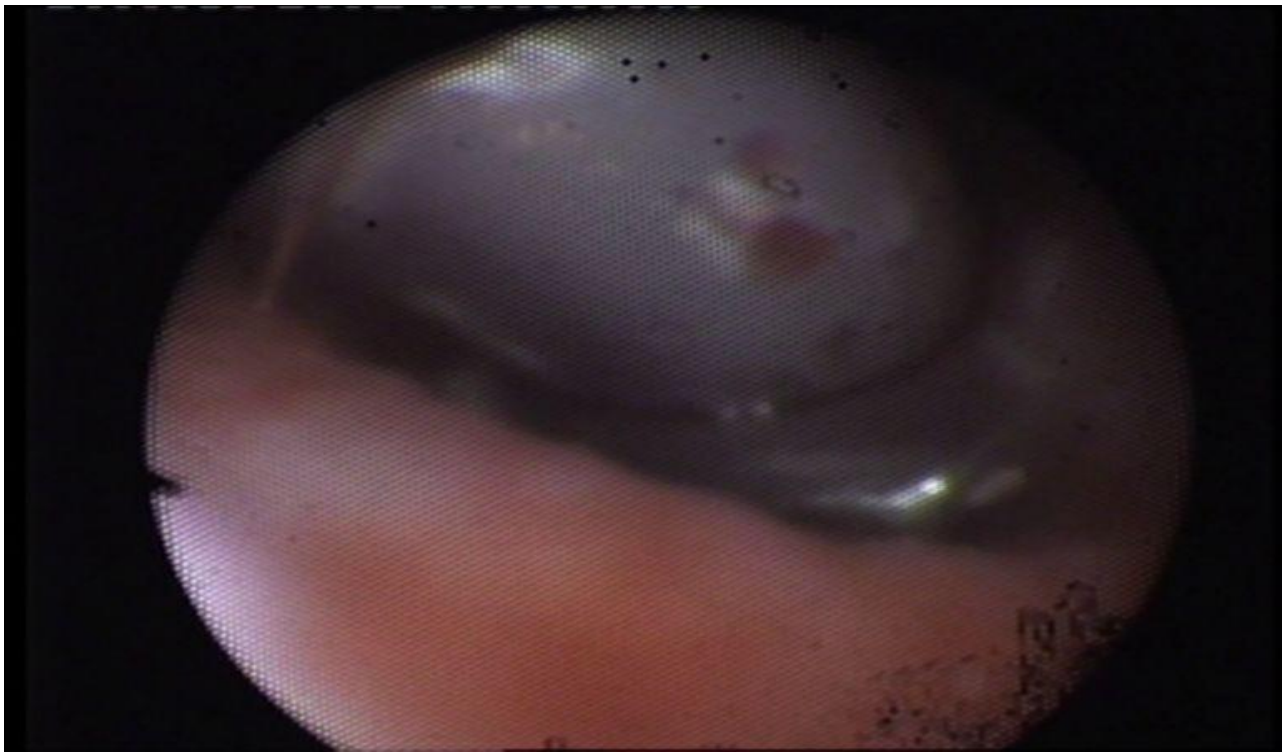
6. The inflation of the balloon produces a traction of the tracheostomy tube towards the inside of the trachea.

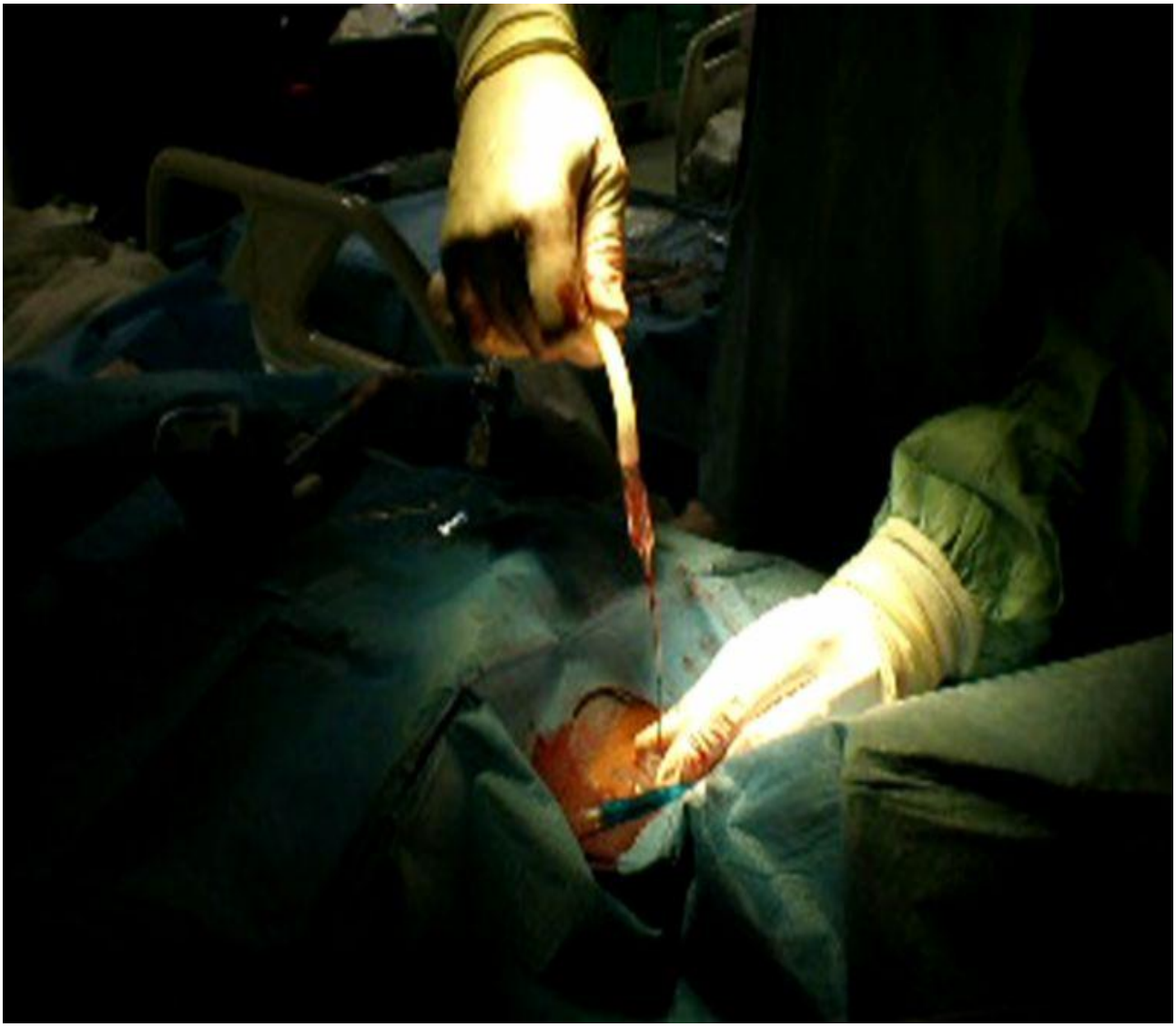


7. After dilation of the tracheal wall, the tracheostomy tube is inserted into the trachea. The dilator tube is still inflated and used as an insertion device.

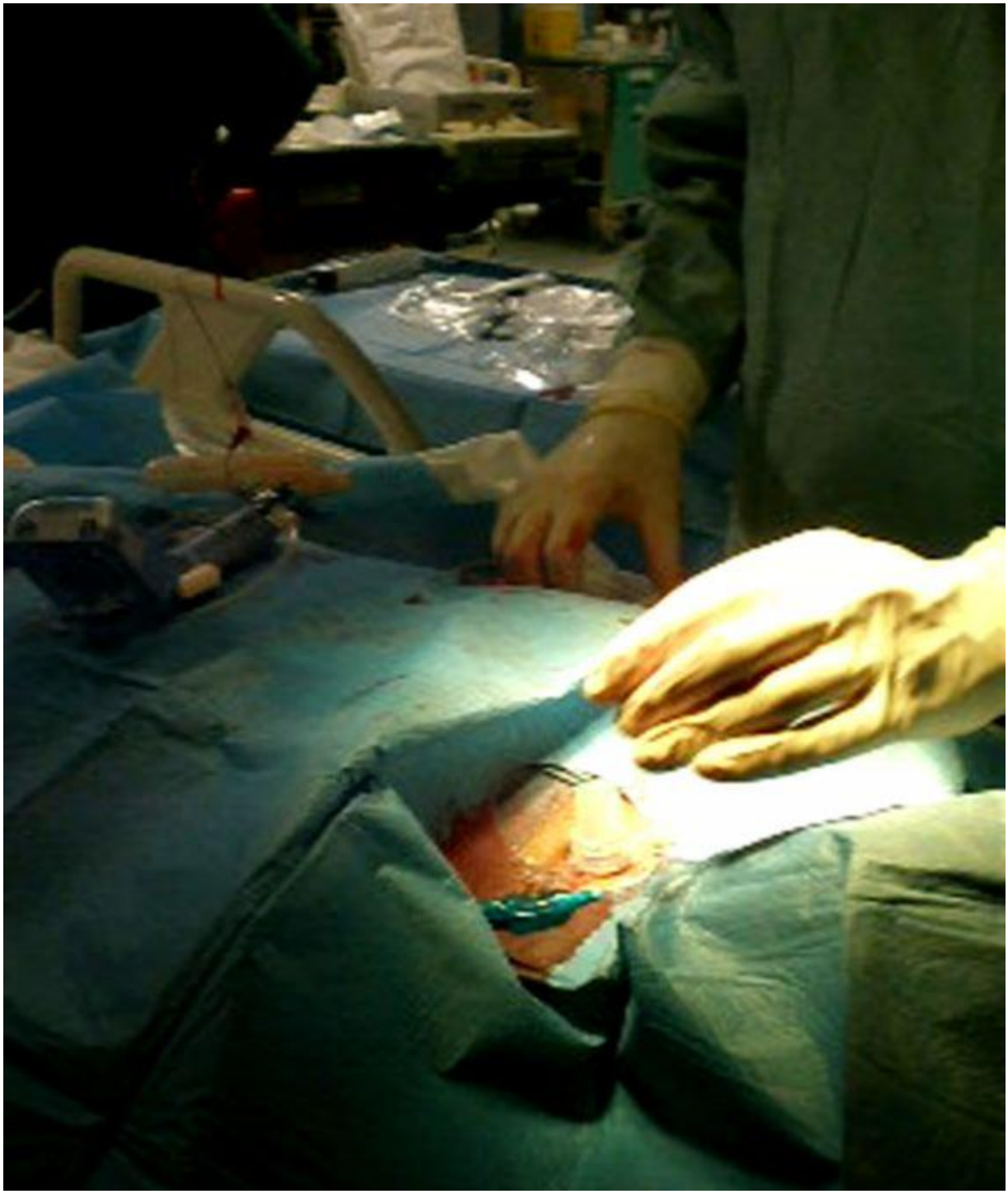


8. The balloon is deflated, leaving the tracheostomy tube in the trachea. Below, the tracheostomy tube positioned in the trachea, seen via the Bronchoscope





9. The G-Trach is removed leaving the tracheostomy tube in the trachea.



9. End of the procedure. The picture shows the tracheal tube positioned inside the trachea.

Conclusions

The limitations of existing PDTs are: i) learning difficulty, ii) percentage and iii) type of complications and iv) time needed to perform the procedures. These considerations led us to develop a new PDT device, more performant, easy to use and safe.

The first experimental stage on the pigs of the new device G-Trach has showed the following advantages:

- The procedure is effective;

- The procedure requires one step less than the other PDT procedures;

The time required for the procedure is about 3 minutes;

- Bleeding was comparable with the other PDTs;

- Minimal changes in vital signs (Mean Systemic Pressure, SaO2. Heart Rate).

The first six tracheostomies on humans have basically confirmed these findings. This study, however, has pointed out the need to modify some features of the G-Trach that have led to a new patent application (GO2011A000004).

Indeed, these first tracheostomies on humans have confirmed the positive aspects of the G-Trach, in particular the initial thrust of the device into the trachea, as well as its straightforward utilisation and learning procedures, thus giving new momentum to the project. However, there has been the need of a skin incision of 15-20mm, comparable with other common techniques, whereas the originally planned procedures were presumed to imply only a minimal incision. This was due to the risk of skin capture between the distal balloon dilator and the tracheotomy tube, thus preventing its progression into the trachea.

This risk was due to the difference in size between the tracheotomy tube and the deflated balloon, a problem that was not detected during the pig trials. Indeed, in pigs the distance between the skin and the trachea is greater than 5 cm. Therefore, as mentioned above, the needle placement was preceded by an incision of the tissues until a distance from the trachea comparable with the size of the tracheotomy tube was reached.

To resolve this problem the G-Trach has been modified so as to provide a smooth transition between the tracheal tube and the balloon dilator. The modified device with a plastic wedge inside

the balloon dilator yielded better results than the previous version but still did not provide a smooth enough continuity in the transition between the balloon dilator and the tracheostomy tube during the progression into the trachea. We believe that to achieve the desired standard of efficiency, i.e. minimal incision of the skin and minimum effort to introduce the tracheal tube, it is necessary to make the modifications proposed in the second patent, specifically as concerns the profile of the balloon inverted cone in such a way that it wraps the tip of the tracheotomy tube. This new profile would allow the balloon, already in the dilative phase of inflation to surpass by a few millimeters the tip of the tube tracheotomy without any effort, thus leaving only a minimal effort to complete the introduction of the tracheal tube into the trachea. Indeed, the need of the tip of the tracheal tube to surpass the tissues and the tracheal rings, in all PDT devices represents the most difficult step, because the force required in this phase brings about a non-negligible risk of tracheal rings rupture. These novelties were presented in a second patent filed in 2011 which, however, confirms and even strengthens the concept of balloon dilator inverted cone. We believe that this development could be substantial and final.

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Annex-1

Anaesthesia. 2012 Sep;67(9):968-72. doi: 10.1111/j.1365-2044.2012.07188.x. Epub 2012 Jun 1.PMID:22670801[PubMed - indexed for MEDLINE] I.F. 2.958

A new technique for percutaneous dilatational tracheostomy (G-Trach): preliminary experience in pigs.

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Summary

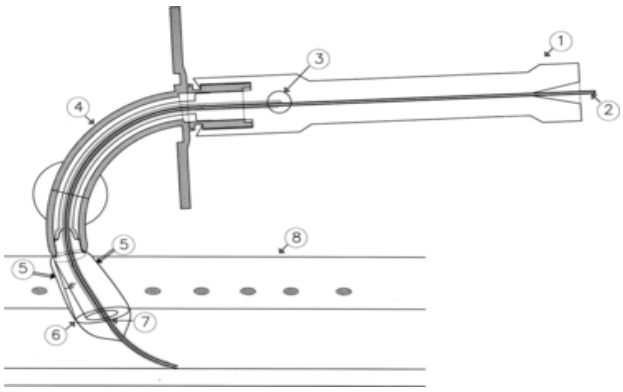
Tracheostomies are currently used for airway management in patients requiring long-term respiratory assistance. The dilatational percutaneous technique of forming tracheostomies is a valuable alternative to traditional surgical 'open' techniques. In this study, we tested a new dilatational percutaneous tracheostomy device using a balloon dilator with a particular innovative shape (G-Trach). At the Autonomous University of Barcelona Veterinary Institute, eight pigs (weighing 20–40 kg) were anaesthetised and underwent tracheostomy using the novel G-Trach technique. The mean (SD) procedure time was 2.63 (0.64) min from tracheal puncture to ventilation through the tracheostomy tube, and the mean (SD) time from positioning the dilator balloon to introducing the cannula was 0.71 (0.38) min. Vital functions and oxygen saturation remained constant throughout the procedures. Postmortem examinations did not reveal any tracheal injury. The G-Trach seems to be a safe and easy new dilatational percutaneous technique for forming tracheostomies. The minimal subcutaneous tissue dissection could potentially decrease complications when compared with standard dilatational percutaneous tracheostomy methods. To confirm this hypothesis a human trial is ongoing.

Over the past 20 years there has been a rapid growth in the use of tracheostomies for the management of patients requiring long-term respiratory assistance in intensive care units (ICUs) [1–3]. Numerous studies have tested low-invasive surgical, percutaneous and trans-laryngeal

techniques to identify safe, efficient and convenient alternatives to the standard ‘open’ surgical tracheostomy [1, 4]. In a comprehensive study of peri-operative complications from the various dilatational percutaneous tracheostomy techniques, Byhahn et al. [5] reported a 23% overall occurrence of complications, with a minimum of 6% for the Ciaglia Blue Rhino® (Cook Medical, Limerick, Ireland) dilator technique. Peri-operative complications most frequently associated with dilatational percutaneous tracheostomy techniques include hypotension, hypoxia, bleeding, resistance to the insertion of the cannula, peritracheal tube insertion (with false passage formation), damage to the posterior tracheal wall and fracture of tracheal rings (the latter accounting for about 25% of all complications) [5, 6]. It is often believed that when performing dilatational percutaneous tracheostomies, tracheal rings are displaced, but remain intact. However, a study on cadaveric specimens has shown substantial peristomal mucosal tears and cartilaginous fractures that may lead to clinically relevant tracheal stenosis [7]. The fracture of tracheal rings may be due to the longitudinal force applied during the dilatation phase of the manoeuvre. One study reports the complication of tracheal ring fractures in 9.5% of cases when using the Ciaglia single dilator technique, the latter being generally considered to be the safest and most widely used of the dilatational percutaneous tracheostomy techniques [8]. A more recent device for dilatational percutaneous tracheostomy utilises a balloon dilation technique imparting a radial force. However, this innovative feature was recently questioned by Cianchi et al. [9] who demonstrated the superiority of the Ciaglia single dilator technique.

With the aim of further improving the safety of percutaneous tracheostomy procedures, we developed a novel dilatational percutaneous tracheostomy device (the G-Trach). The innovative characteristic of the G-Trach is a balloon dilator shaped as an inverted cone, with the distal diameter being larger than the proximal diameter (Fig. 1). Due to the design characteristics, the G-Trach is theoretically less harmful to the tracheal rings than other methods currently employed when performing dilatational percutaneous tracheostomies; it could, therefore, reduce the number of complications associated with the procedure. In this preliminary study, we tested the G-Trach device on healthy pigs to evaluate the feasibility of the procedure and its potential advantages over conventional techniques.

Figure 1. Longitudinal annotation of the G-Trach device. Note the inverted cone shape of the dilator balloon (6) with its proximal part partially inside (1–2 cm) the tracheal tube. The device incorporates the handle (1), the wire guide (2), and the balloon inflating tube that ends in the distal part of the balloon (3 & 7). The tracheal tube (4), the guidewire (2) and the skin surface (8) are also represented.

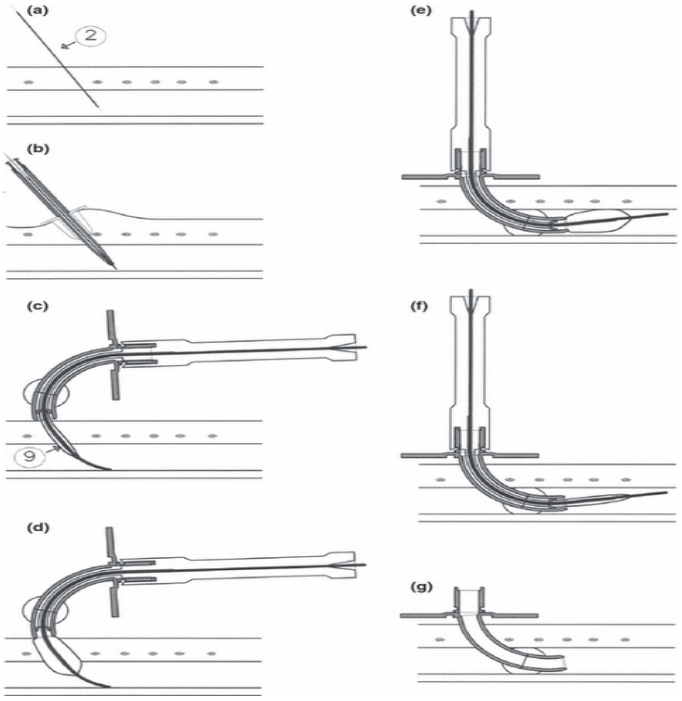


Methods

The study was carried out on eight adult pigs (weighing 20–40 kg body mass) at the Veterinary Institute of the Autonomous University of Barcelona in accordance with the institutional guidelines on animal welfare. The protocol was approved by our Institutional Review Board.

As mentioned above, the G-Trach is characterised by an inverted cone-shaped dilator balloon that is inflated by an inflating tube ending in the distal part of the dilator balloon (Fig. 1). During inflation this shape facilitates the progression of the balloon along the tracheal tissues. In addition, the inflation of the distal part opens the tracheal rings from inside by compressing the tissue against the tracheostomy tube. The G-Trach allows for a genuinely single-step procedure: the tracheostomy tube, which is firmly attached to the proximal part of the balloon and to the handle, is introduced with the G-Trach apparatus by the operator once the balloon dilator has been inflated (Fig. 2).

Figure 2. The sequence for G-Trach insertion: a: After puncture of the anterior tracheal wall by a needle, the guidewire is inserted through the needle bore (2); b: Insertion of the small dilator over the guidewire; c: Introduction of the G-Trach apparatus along the guidewire across the tracheal wall with the tracheostomy tube hooked to the handle. The deflated balloon is introduced through the anterior tracheal wall (9); d: Balloon inflation. The expansion forces during inflation (7–10 atmospheres) facilitates introduction of the tube into the trachea; e: After dilation of the tracheal wall, the tracheostomy tube is inserted into the trachea. The dilator tube is still inflated and used as an insertion device; f & g: After balloon deflation, the G-Trach apparatus is removed leaving the tracheostomy tube in the trachea.



The animals received premedication with intramuscular morphine 0.4 mg.kg^{-1}, ketamine 10 mg.kg^{-1} and azaperone 4 mg.kg^{-1}. Anaesthesia was induced using 10 mg.kg^{-1} of intravenous thiopental, following which the animals underwent tracheal intubation. Anaesthesia was maintained using inhaled isoflurane at 2%. Heart rate, blood pressure and arterial blood oxygen saturation were monitored by catheterisation of the femoral artery. After evaluation of the anatomic aspects of the throat and an injection of lidocaine 1%, a 17-G cannula was inserted between the first tracheal rings. In the four largest pigs (40 kg) in whom the distance between the skin and the trachea was greater than 4 cm, needle placement was preceded by an engraving of the rind to achieve a depth to the trachea of 3.5–4.0 cm compatible with the length (5.0 cm) of the dilator balloon of the G-Trach device. A needle was used to estimate the correct engraving depth. A guide wire of 0.38 mm diameter was then positioned through the needle into the trachea (Fig. 2a). In the other four pigs, a longitudinal 3-cm incision of the skin was performed with a scalpel and was followed by insertion over the guidewire of a 14-F dilator to facilitate the insertion of the deflated balloon (Fig. 2b). A large amount of lubricant was used before insertion of the balloon and the cannula. The dilator balloon of the G-Trach, loaded with a tracheostomy tube of 8.5 mm internal diameter (Rusch Tracheofix™, Teleflex Medical, Varedo, Italy), was then introduced into the trachea and inflated with 15–20 ml saline 0.9% to a pressure of 7–10 atmospheres using a locking syringe equipped with a pressure gauge (Figs 2c & 2d). After inflation only a little force was exerted on the handle to allow the introduction of the cannula (Fig. 2e). Once the tracheostomy tube was positioned, the balloon was immediately deflated and removed leaving the tracheostomy tube in place (Figs 2f & 2g). A photograph of the equipment used is shown in Fig. 3.

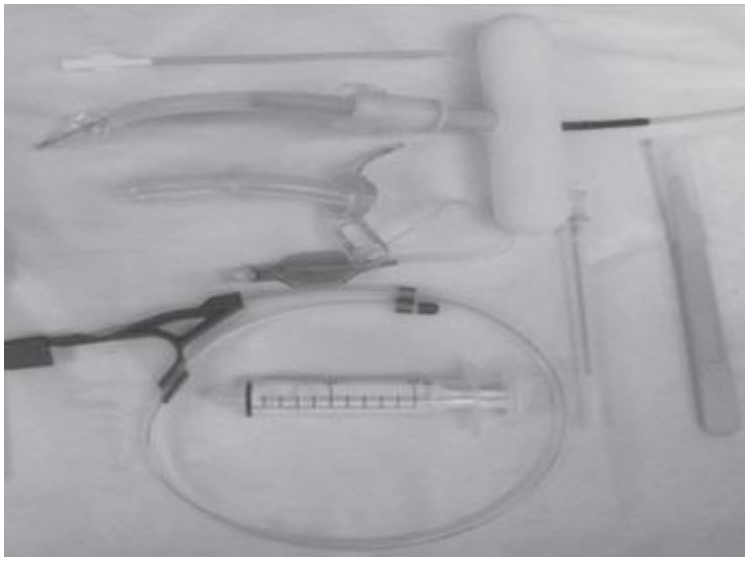


Figure 3. The G-Trach equipment used. (a) 14-F dilator; (b) the G-Trach device; (c) tracheostomy tube; (d) metallic guidewire; (e) 17-G needle; (f) scalpel; (g) locking syringe.

After removal of the orotracheal tube, the pigs' lungs were ventilated for 5–10 min via the tracheostomy tube. Following this they were euthanised and their tracheas opened to evaluate the correct position of the cannula, the presence of any posterior wall tracheal injuries, and any broken tracheal rings. The size of the trachea was also measured by means of a feeler gauge.

Results

The mean (SD) time from tracheal puncture to ventilation through the tracheostomy tube was 2.63 (0.64) min. The mean (SD) time for inflating the balloon, dilating the subcutaneous and tracheal tissues, and introducing the cannula was 0.71 (0.38) min. There was no visible bleeding from the tracheostomy site, either externally or into the trachea. The post-tracheostomy ventilation and postmortem evaluations confirmed correct positioning of the cannula. Neither injuries to tracheal rings and posterior trachea wall, nor occult bleeding were detected at postmortem trachea examination. In all the eight pigs, heart rate, rhythm, blood pressure and arterial oxygen saturation did not change significantly during the procedure (Table 1). The internal diameter of the pigs' trachea ranged from 12 to 15 mm.

Table 1. Heart rate, blood pressure and arterial oxygen saturation measured in pigs before (baseline) and during the procedure. Values are mean (SD).

	Baseline	Procedure	p value
Heart Rate (bpm)	**88.2 (8.1)**	**92.8 (11.7)**	**0.121**
MAP (mmHg)	**69.0 (4.5)**	**73.2 (6.2)**	**0.081**
SaO2 (%)	**97.0 (1.1)**	**95.8 (3.2)**	**0.108**

1. MAP, mean arterial pressure; SaO_2, arterial oxygen saturation.

Discussion

The complications associated with dilatational percutaneous tracheostomy procedures are, without doubt, fewer than those associated with the traditional surgical tracheostomy technique [4]. Nevertheless, significant complications are still reported with the use of the various commercially available devices for dilatational percutaneous tracheostomy [7]. Rupture of the tracheal rings and injury to the posterior wall of the trachea are the most frequent and dangerous complications described [6–8]. These complications are partially due to the downward and longitudinal forces applied to the surrounding tissues and posterior tracheal wall during the dilation phase of the Ciaglia single dilator technique. Conversely, the G-Trach dilator balloon system applies a radial force to the peritracheal structures that ought to dilate the tracheal rings without tearing or damage. Moreover, the absence of downward force associated with the use of the balloon dilator system reduces the risk for posterior wall injuries. The same advantages have been postulated for a dilatational percutaneous tracheostomy device using the balloon technique for dilation (Blue Dolphin, Cook) [10]. The G-Trach differs from this latter device in the shape of its balloon which we believe introduces some potential major technical improvements. The inverted-cone shape of our device facilitates a quick introduction of the cannula into the trachea after inflation of the dilator balloon. The mean (SD) time required for the introduction of the cannula was 0.71 (0.38) min), a substantial shortening of the overall time normally required for the procedure, thus reducing the risk of hypoxia. In addition, since the dilation was followed by insertion of the tracheal tube without interruption, the peritracheal tissues were kept constantly under pressure with a potential reduced risk of bleeding.

Pigs were used to test this technique because the anatomy and size of pig tracheas are similar to those in humans. Based on our experience, the average depth from the skin to the trachea is about 1–2.5 cm in ICU patients. In our pigs, the depth between the skin and the trachea varied from 3 to 6 cm. This, together with the greater tracheal collapsibility in pigs, makes the procedure somewhat complicated in these animals; we therefore expect a higher probability of success in humans.

In conclusion, this first experience in eight pigs showed that G-Trach system can be used safely for the placement of a tracheostomy tube. Moreover, the G-Trach appears to be easy and quick to use, and offers potential advantages compared with the methods currently used for dilatational percutaneous tracheostomy. These potential advantages need to be shown in humans and an appropriate trial is ongoing. If this technique proves to be equally effective in humans as it was in our animal cohort, we believe its represents a concrete step forward in reducing the morbidity associated with the current procedures for dilatational percutaneous tracheostomy.

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Annex 2

2° Congresso Nazionale sulla Medicina di Genere. Ottobre 2010 Padova libro degli Abstracts, pg 45

LIVELLI DI OMOCISTEINA E FOLATI IN GIOVANI DONNE ITALIANE.

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SCOPO. L'omocisteina (HCY) è un nuovo biomarcatore non tradizionale di rischio di malattia cardiovascolare (CVD), che aumenta notevolmente nelle donne in post-menopausa, quindi, è un potenziale marker di rischio di CVD nelle donne. C'è scarsità di dati sui livelli e sulla modulazione della HCY in giovani donne. In particolare, la modulazione di HCY dovuta alla attività fisica sportiva eseguita a livelli non professionali nelle donne sane è in gran parte inesplorata.

METODI. Abbiamo valutato l'influenza della attività fisica sportiva ricreativa in giovani donne sane su HCY, un fattore di rischio per CVD potenzialmente prevenibile. Le partecipanti erano 124 atlete di età media 23 anni, (che eseguono 8,7 ± 2,46 ore/settimana di esercizio) e 116 controlli sedentari matched.

RISULTATI. La concentrazione mediana di HCY, folato e marcatori lipidici non differisce tra le atlete e i controlli. Livelli elevati di HCY a rischio CVD ≥ 12,0 micromol /L e ≥ 15,0 micromol/ L non differivano tra i 2 gruppi. L'omocisteina è risultata essere inversamente proporzionale al folato (P <0,001), positivamente correlata con l'età (P = 0,009) e con la creatinina (P = 0.033), ma non è risultata essere associata con le ore di attività fisica, indice di massa corporea (BMI) e marcatori lipidici. Le donne con deplezione di folati (<3.0 mg/L) hanno avuto una probabilità di 4,5 volte di

avere HCY ≥ 15,0 micromol/L.

CONCLUSIONI. L'esercizio fisico non ha impatto negativo sui livelli di omocisteina tra le giovani donne. Solo i folati bassi aumentano significativamente il rischio di iper-omocisteinemia nelle giovani donne. Ne risulta che una maggiore attenzione ai livelli di folato nelle donne giovani è fortemente raccomandata.

FINANZIAMENTO. Università degli Studi di Udine, Italia.

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2°Congresso Nazionale sulla Medicina di Genere. Ottobre 2010 Padova, libro degli Abstracts, pg 45

MODULAZIONE DELLA PROTEINA C-REATTIVA AD ALTA SENSIBILITÀ DOVUTA A CONTRACCETTIVI ORALI IN GIOVANI DONNE ITALIANE.

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SCOPO. Diverse evidenze recenti documentano una diversità di genere nei livelli plasmatici della proteina C-reattiva ad alta sensibilità (hsCRP) in adulti sani. Lo scopo di questo studio è di valutare l'impatto dei contraccettivi orali (OC) sui livelli di hsCRP e lipidi nella popolazione di giovani donne fertili, non obese italiane.

METODI. I diversi biomarcatori sono stati valutati nel sangue venoso di 277 donne sane bianche italiane (23 anni di età, indice di massa corporea 21 kg/m2). 77 utilizzatrici di OC sono state confrontate con 200 non-utilizzatrici. Sono stati esaminati cutoff progressivi di hsCRP.

RISULTATI. I livelli di hsCRP ad alto rischio di malattie cardiovascolari (da 3,0 a <10,0 mg / L) sono stati trovati nel 27,3% delle utilizzatrici di OC e nel 8,5% delle non-utilizzatrici [odds ratio (OR) 4.04; CI 1,99-8,18]. I livelli di hsCRP a rischio intermedio (da 1.0 a <3,0 mg / L) sono stati trovati in 32,5% delle utilizzatrici di OC e 11,0% delle non-utilizzatrici (OR 3,89; CI 2,03-7,46). In particolare, le non-utilizzatrici avevano una probabilità di 8,65 (CI 4,39-17,1) volte maggiore di dimostrare un livello protettivo di hsCRP (<0,5 mg / L) rispetto alle utilizzatrici OC. L'uso di OC

provoca aumento dei trigliceridi nel siero (P <.001) e di colesterolo totale P =. 001), tuttavia, è il colesterolo HDL a provocare questo aumento. È interessante notare che un minore rapporto LDL /HDL è stato osservato in utilizzatrici di OC rispetto alle non-utilizzatrici (P =.016).

CONCLUSIONE. L'uso di OC aumenta lo stato infiammatorio di basso grado come misurato dalle concentrazioni di hsCRP. L'alterazione dello stato infiammatorio nelle utilizzatrici di OC potrebbe influire sul rischio di tromboembolia venosa, malattie cardiovascolari e altre condizioni avverse nelle giovani donne. Visti gli effetti della contraccezione ormonale sullo stato infiammatorio e rischio cardiovascolare è probabile che la contraccezione ormonale sia una rilevante componente della disparità di genere nel CVD che si dovrebbe tenere in maggiore considerazione.

FINANZIAMENTO. Università degli Studi di Udine.

42° Congresso Nazionale SIBioC 2010 Roma,BC Biochimica Clinica 34,446,2010- libro degli Abstracts

CARDIAC INJURY MARKERS IN NON-ELITE ULTRAENDURANCE RUNNERS.

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Introduction. An elevation of cardiac injury markers including creatinine kinase (CK), myoglobin (Myo) and cardiac troponin (cTn) especially cTnT has been observed in elite athletes following strenuous exercise. The mechanism and significance of this observation however have not been fully elucidated.

Aim. The goals of this study were: 1) to determine the kind and amount of changes in plasma biomarkers in non-elite athletes; and 2) to identify possible clinical or biochemical associations.

Methods. We recruited 10 non-elite runners in 2009, performing a 3 days long race (23 km on day 1, 49 km on day 2 and 19 km on day 3). Demographic data and blood samples were collected for analysis of CK, CKMBm, Myo, cTnI, and Creatinine (Cr) levels within two hours of race start (baseline), at race completion, and 5 days post-race.

Results. All subjects exhibited significant elevations in Myo ($P < 0.001$) , CK ($P < 0.001$), CKMBm ($P < 0.001$), cTnI ($P = 0.03$) and Cr ($P = 0.02$) immediately postrace. However, the CKMBm/CK ratio did not differ. All biomarkers returned to baseline (pre-race) values 5 dayspost race.

Conclusion. Dramatically elevated values of plasma biomarkers normally associated with cardiac damage likely do not indicate real cardiac injury as highlighted by the absence of CKMBm/CK variation. The modest elevation in cTnI levels post-race is likely a non-specific phenomenon in marathon runners. However, whether the increase in the levels of these enzymes represents true subclinical myocardial injury or a result of the release of cTnI from the myocytes (or other cells) requires further investigation.

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44th National Congress of the Italian Society of Clinical Biochemistry and Clinical Molecular Biology

ORAL CONTRACEPTIVE USE INCREASES CHRONIC INFLAMMATION IN YOUNG FEMALE ATHLETES

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BACKGROUND— Chronic activation of innate immune system may play a crucial role in pathophysiology of several diseases including cardiovascular disease (CVD) and type 2 diabetes mel-litus. Exercise training has been shown to have anti-inflammatory effects. However, the use of oral contraceptives (OCs) by fertile female athletes has the potential to increase low-grade chronic inflammation [1]. The increase of basal inflammatory status can hamper protective effects of training and can be potentially det-rimental to athletic performance, which is commonly associated with inflammatory lesions. There are limited data exploring the effects OC use by athletes. Our aims were to evaluate the impact of OCs currently used by female athletes on levels of hsCRP, triglicerides and cholesterol in a population of young white female athletes.

METHODS AND RESULTS — We compared the association between OC use and hsCRP across 4groups (OC user athletes, non-OC user athletes, OC user non-athletes, non-OC user non-athletes). A total of 277 young healthy Caucasian Italian women [mean age, 23 years (SD, 5 years); body mass index (BMI), 21 kg/m2 (SD, 2 kg/m2] were analyzed. Progressive cutoffs of hsCRP lev-els were evaluated in OC users (n = 77, 27.8%) compared to non-OC users (n = 200, 72.2%). Levels of hsCRP at high risk of future cardiovascular events from 3.0 to < 10.0 mg/L were found in 27.3% (21/77) of OC users and in 8.5% (17/200) of non-OC users [odds ratio (OR) = 4.0, P < 0.001]. No differences were observed between athletes and non-athletes.

CONCLUSIONS—OC use markedly increases chronic low-grade inflammatory status in athletes as assessed by the increase of serum hsCRP. Our findings suggest that OC use may elevate CVD risk

and predispose to a higher inflammatory response to physical stress and injury.

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FORT ASSAY: A RAPID METHOD TO DETERMINE OXIDATIVE STRESS DURING PROLONGED EXERCISE IN PATIENTS WITH TYPE 1 DIABETES

44th National Congress of the Italian Society of Clinical Biochemistry and Clinical Molecular Biology. Abstracts

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BACKGROUND.

Oxidative stress is a widely accepted component in the development and progression of type 2 diabetes and its complications. However, inconsistent results have been reported in patients with type 1 diabetes (T1DM) for all the commonly measured markers of oxidative stress. Physical activity is widely encouraged to the T1DM patients; however, the impact on oxidative stress in these patients is largely unknown. We aimed at investigating the impact of prolonged moderate exercise oxidative stress during in a group of T1DM patients and a group of well-matched healthy controls.

METHODS. Nine patients (47±10 years, 73±15 kg, 170±10 cm; Hba1c 7.1±1.1%) and 15 healthy controls (46±10 years, 75±16 kg,174±10 cm) performed a 3-hrs constant intensity walk at 30% of the heart rate reserve. Patients were administered appropriate amounts of carbohydrates to avoid an excessive fall of glycemia [1, 2]. Venous blood samples were obtained before and at the very end of the trials for determination of glucose by means of a hexokinase based methodology (Olympus Diagnostic Systems AU2700) and insulin levels, which included the exogenous administered insulin by Immunoassay system (Beckman Coulter, Fullerton, CA). Capillary blood samples (n = 240) were taken in duplicate at the start and the very end of the walks and as single measurements every 30 min throughout the exercise to perform the Free Oxygen Radicals Test (FORT, CR-2000 Callegari1930, Italy).

RESULTS. Glucose and insulin levels were higher in patients than in controls. Type 1 DM patients

showed higher oxidative stress values as compared to healthy controls (380.1±14.7 vs 293.1±9.6 arbitrary units; $p < 0.05$). Nevertheless, oxidative stress remained constant in both groups of volunteers throughout the whole exercise (p = NS).

CONCLUSIONS. The FORT assay is actually an easy method to
determine the oxidative stress also during exercise. Our study showed higher oxidative stress values in type 1 diabetic patients show as compared to healthy people. Nevertheless, prolonged moderate exercise does not exacerbate this potentially harmful condition.

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Constancy of oxidative stress during prolonged exercise in insulin-dependent diabetic patients.

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Abstract

Dept of Medical and Biological Sciences, Univ. of Udine, Italy Diabetes mellitus (DM) is accompanied by increased formation of free radicals and decreased antioxidant capacity, leading to oxidative stress. Current management of DM includes physical activity, but the impact of prolonged exercise on oxidative stress is unclear. We investigated the oxidative stress during prolonged moderate exercise in a group of insulin-dependent patients and a group of well-matched healthy controls. Nine patients (47±10 years, 73±15 kg, 170±10 cm; Hba1c 7.1±1.1%) and 15 controls (46±10 years, 75±16 kg, 174±10 cm) performed a 3-hrs constant intensity walk at 30% of their heart rate reserve. Patients were given appropriate amounts of sucrose to avoid hypoglycemia. Venous blood samples were obtained prior to and after the walks to determine glucose and insulin levels. The FORT test (Callegari1930, Italy) was performed on capillary blood at the start and thereafter at 30 min intervals. Glucose and insulin levels were higher in patients than in controls ($p<0.05$ both prior to and after the exercise). Patients showed higher oxidative stress values as compared to healthy controls (380.1±14.7 vs. 293.1±9.6 a.u.; $p<0.05$). Oxidative stress remained constant in both groups throughout the exercise (p=NS). In conclusion, even if patients usually show higher oxidative stress values than healthy people, prolonged moderate exercise does not exacerbate this potentially harmful condition.

Oxidative Stress During Prolonged Exercise in Insulin-Dependent Type 1 Diabetic Patients

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Background. Several studies showed that diabetes mellitus (DM) is accompanied by increased formation of free radicals and decreased antioxidant capacity, leading to oxidative stress. Physical activity is part of the management of DM; however, the impact of exercise on oxidative stress is unclear. We aimed at investigating the oxidative stress during prolonged moderate exercise in a group of type 1 DM patients and a group of well-matched healthy controls.

Methods. Nine patients (47 ±10 years, 73 ± 15 kg weight, 170 ± 10 cm stature; Hba1c 7.1 ± 1.1%) and 15 healthy controls (46 ± 10 years, 75 ± 16 kg weight, 174 ± 10 cm stature) performed a 3-hrs constant intensity walk at 30% of the heart rate reserve. Patients were administered appropriate amounts of carbohydrates to avoid an excessive fall of glycemia. Venous blood samples were obtained before and at the very end of the trials for determination of glucose and insulin levels. Capillary blood samples were taken at the start of the walks and thereafter every 30 min to perform the Free Oxygen Radicals Test (FORT, CR-2000 Callegari1930, Italy).

Results. Glucose and insulin levels were higher in patients than in controls. Type 1 DM patients showed higher oxidative stress values as compared to healthy controls (380.1 ± 14.7 vs 293.1 ± 9.6 arbitrary units; $P < 0.05$). Nevertheless, oxidative stress remained constant in both groups of volunteers throughout the whole exercise (P = NS).

Conclusions. The illustrated data show that, even if type 1 diabetic patients show higher oxidative stress values as compared to healthy people, prolonged moderate exercise does not exacerbate this potentially harmful condition.