Table 1. Patient and Transplant Characteristics, Authorisations

PATIENTS	**CASE 1**	**CASE 2**	**CASE 3**
Residency	Iceland	USA	Turkey
Gender	Male	Male	Female
Age at Primary Procedure	36	30	22
Etiology of Tracheal disorder	Malignancy? (not verified) Relapse of Tracheal Mucoepidermoid Carcinoma?	Malignancy, Tracheal Adenoid Cystic Carcinoma	1st Transplantation Iatrogenic Injury 2nd (Re)-transplantation Material Fatigue/ Collapse of the previous Synthetic Tracheal Transplant
PRIMARY PROCEDURE	**SYNTHETIC TRACHEA**	**SYNTHETIC TRACHEA**	**PULMECTOMY + SYNTHETIC TRACHEA**
Date of Procedure	Jun 9, 2011	Nov 17, 2011	Aug 7, 2012
Pre-operative Hospitalization	No	No	No
Type of Surgery (planned months in advance)	Elective	Elective	Elective
Scaffold Material (Synthetic)	Nanocomposite polymer (POSS-PCU; polyhedral oligomeric silsesquioxane [POSS] covalently bonded to poly-[carbonate-urea] urethane[PCU])	Electrospun polyblend of PET/PU 70/30; polyethylene terephthalate (PET) and polyurethane (PU)	Electrospun polyblend of PET/PU 70/30 nanofibers; polyethylene terephthalate (PET) and polyurethane (PU)
CE Marking	No	No	No
Scaffold Manufacturer	Prof. Seifalian, University College London, UK	Nanofiber Solutions, Ohio, USA	Nanofiber Solutions, Ohio, USA
Import of Scaffold to Sweden	Private	n/a	n/a
“Off label ”Use of Growth Factors and Bone Marrow Stimulating Drugs in “Supra-therapeutic” Doses	Yes	Yes	Yes
Application for Vetting of the Ethics to the Regional Ethical Review Board	No	No	No
Application to the Swedish Medical Products Agency	n/a	n/a	n/a
Reporting of Transplant Related Side-Effects and Complications to Swedish Medical Products Agency	n/a	n/a	n/a
SECONDARY PROCEDURE	**-**	**-**	**RE-TRANSPLANTATION SYNTHETIC TRACHEA**
Date of Procedure	-	-	Jul 9, 2013
Pre-operative Hospitalization	-	-	Yes
Type of Surgery (planned months in advance)	-	-	Elective
Scaffold Material (Synthetic)	-	-	Electrospun PET; polyethylene terephthalate (PET)
CE Marking	-	-	No
Scaffold Manufacturer	-	-	Harvard Apparatus Regenerative Technology, HART, Holliston, MA, USA
Import of Scaffold to Sweden	-	-	n/a
“Off label ”Use of Growth Factors and Bone Marrow Stimulating Drugs in “Supra-therapeutic” Doses	-	-	Yes
Application for Vetting of the Ethics to the Regional Ethical Review Board	-	-	No
Application to the Swedish Medical Products Agency	-	-	n/a
Reporting of Transplant Related Side-Effects and Complications to Swedish Medical Products Agency			n/a

Table 2. Etiology of Tracheal Disorder and Transplantation-associated Drugs

PATIENTS	**CASE 1** Transplantation Jun 9, 2011	**CASE 2** Transplantation Nov 17, 2011	**CASE 3** **1st Transplantation** Aug 7, 2012	**CASE 3** **2nd Transplantation** Jul 9, 2013
Etiology of Tracheal Disorder	Malignancy? (not verified) Relapse of Tracheal Mucoepidermoid Carcinoma?	Malignancy, Tracheal Adenoid Cystic Carcinoma	Iatrogenic Injury	Material Fatigue/ Collapse of the previous Synthetic Tracheal Transplant
Histological Verification of Malignancy before/after Transplantation registered in the Medical Records	No	Yes		
Surgical RADICALITY of Tumour Resection at Native Tracheal Extirpation and Synthetic Tracheal Transplantation	n/a (NO registered postop histological analysis of native trachea in the Karolinska records)	No (surgical radicality was not achieved at extirpation of native trachea)		
TRANSPLANTATION ASSOCIATED DRUGS				
Application to Medical Products Agency	n/a	n/a	n/a	n/a
Application to Reg. Ethical Review Board	No	No	No	No
"OFF LABEL" – EXPERIMENTAL USE (Indication and Dosage) of Growth Factors and Bone Marrow Stimulating Drugs in "Supra-therapeutic" Doses	Yes (despite previous malignant tumor)	Yes (despite non-radical extirpation of malignant tumor)	Yes	Yes
Recombinant Human Transforming Growth Factor-β3 Manufacturer: R&D Systems, Minneapolis, MN, USA. **RESEARCH USE ONLY, NOT FOR USE IN HUMANS OR ANIMALS ACCORDING TO MANUFACT**	Yes **Perioperative** Dose 10ug/kg cm2 (Scaffold)	n/a (presumably, but not r in the medical records)	n/a (presumably, but not found in the medical records)	n/a (presumably, but not found in the medical records)
Filgrastim, Granulocyte Colony Stimulating Factor (G-CSF) Neupogen® Manufacturer: Amgen Europe BV, Breda, Netherlands	Yes **Perioperative + Postoperative** 20.000.000 U every other day for 10 d. **WEEKLY DOSE 80.000.000 U**	Yes **Perioperative? Postoperative** 20.000.000 U every other day for 15 d. **WEEKLY DOSE 80.000.000 U**	Yes **Perioperative? Postoperative** 20.000.000 U every other day for 16 d. **WEEKLY DOSE 80.000.000 U**	Yes **Perioperative? Postoperative** 30.000.000 U every other day for 14 d. **WEEKLY DOSE 120.000.000 U**
Epoetin beta (synthetic analogue of Erythropoietin) NeoRecormon® Manufacturer: Roche, Grenzach-Wyhlen, Germany. **THE MAXIMUM DOSE FOR LABELED INDICATIONS SHOULD NOT EXCEED 60,000 IU PER WEEK ACCORDING TO MANUFACT**	Yes **Perioperative + Postoperative** 40.000 IU every other day for 12 d. **WEEKLY DOSE 160,000 IU**	Yes **Perioperative n/a Postoperative** 40.000 IU every other day for 15 d. **WEEKLY DOSE 160,000 IU**	Yes **Perioperative + Postoperative** 40.000 IU every other day for 16 d. **WEEKLY DOSE 160,000 IU**	Yes **Perioperative n/a Postoperative** 40.000 IU every other day for 14 d. **WEEKLY DOSE 160,000 IU**
Complications	Yes **RIGHT MAIN PULMONARY ARTERY THROMBUS** (occlusion of the right main pulmonary artery graft interponate that was inserted during the transplantation due to vascular	Yes **VENOUS THROMBOSIS** in the left jugular, subclavian and axillary vein systems + Pulmonary Embolus in left underlobe is diagnosed on the last day of treatment	No	Yes **PUMP-THROMBOSIS** on Extracorporeal Membrane Oxygenation (ECMO) support (extremely rare complication in modern ECMO circuits) > Massive Hemolysis, Acute

	injury of the right pulmonary artery) is diagnosed 9 days after start of treatment			Tub. Necrosis, Acute Renal Failure > 7 weeks of Hemodialysis **+ ARTERIAL EMBOLUS RIGHT LEG** diagnosed 7d. after start of treatment
Long term Complications	Yes Chronic occlusion of RT pulm. Artery + multiple distal PE	No	No	Yes Chronic Renal Failure Cystatine GFR 45-55mL/min/1,73m^2

Table 3. Transplant-related and General Complications, Final outcome

TRANSPLANT RELATED COMPLICATIONS	**CASE 1**	**CASE 2**	**CASE 3**
Transplant associated granulations	Yes (significant)	Yes (scantly)	Yes (significant)
Anastomotic (transplant) dehiscence	Yes (all anastomosis, disconnected transplant)	? (see under tracheo-mediastinal fistula)	Yes (distal anastomosis)
Tracheo-esophageal fistula	Yes	No	Yes
Tracheo-mediastinal fistula	Yes	Yes (suspected in CT report 28 Nov, 2011 and Jan 10, 2012)	Yes (massive air leakage out of thoracotomy)
Near fatal airway (stent) occlusion	Yes (terminally)	No	Yes (multiple occasions)
Normal airway epithelium in transplant	No	No	No
Transplant material fatigue/collapse	No	No	Yes
Thrombo-embolic (TE) events	Yes (RIGHT PULM ART. OCCLUSION + THROMBOSIS of left brachioceph, jugular and subclavian veins + MULTIPLE DISTAL PULMONARY EMBOLIES)	Yes (VENOUS THROMBOSIS in left Jugular, subclavian and axillary vein systems + PULMONARY EMBOLUS in left lower lobe)	Yes (2 TE-events: ECMO PUMP THROMBOSIS + PERIPHERAL ARTERIAL EMBOLIZATION)
Re-transplantation	No	No	Yes (due to material fatigue in 1st transplant)
Chronic infection	Yes (mediastinitis, abscess)	-	Yes (thoracic rest cavity)
Laryngeal nerve paralysis (left sided)	Yes	No	No
GENERAL COMPLICATIONS			
Respiratory failure	Yes	Yes	Yes
Pneumonia (P), Wound infection (W)	Yes (Chronic P)	Yes (P, W)	Yes (P)
Sepsis	Yes	Yes	Yes
Hemoptysis	Yes	Yes	No
Acute (A) Chronic (C) Renal Failure	Yes (A) (terminally)	No	Yes (A, C)
Splenic Infarction	No	No	Yes
Multiple Organ Dysfunction Syndrome	Yes (terminally)	No	Yes
POST-TRANSPLANT INTERVENTIONS/THERAPY			
Airway/Transplant stenting (multiple interventions)	Yes	No	Yes
Bronchoscopy dependency	Yes (intermittent)	No	Yes (every 4th hour, 24-7)
Recurrent extirp of transplant assoc granuloma	Yes	n/a	Yes
Chronically Tracheotomized	No	No	Yes (> 2 years)
Esophageal stenting	Yes	No	Yes
Esophagectomy	Yes (stapled transection)	No	Yes
Esophageal Reconstruction	Yes (subcutaneous colon interponate)	No	Yes (planned for colon interponate)
Thoracoplasty incl. Pedicled m. Lat. Dorsi Flap	No	No	Yes
Chronic Thoracic Drainage	No	No	Yes (2 drainages > 2 years, daily aspiration)
Nutrition through PEG/Gastrostomy	Yes (partly)	No	Yes (2 years)
Laparotomy	Yes	No	Yes (3 times)
Chronic Antibiotic/Antifungal therapy	Yes (intermittent)	No	Yes (> 2 years)
Extracorporeal Membrane Oxygenation	No	No	Yes (3 times, in tot. 72 d.)

Hemodialysis	No	No	Yes (7 weeks)
Prolonged ventilator dependency	Yes	No	Yes (305 days)
FINAL OUTCOME			
Dead/Alive, Date	Died Jan 30, 2014 (after 8 months of hospitalization)	Died Mar 5, 2012	Alive (hospitalized in the ICU after more than 26 months)
Cause of Death	Refractory respiratory insufficiency, total transplant disconnection	Airway bleeding Tracheo-arterial fistula?	-
Total numbers of Transplant Associated Surgical Interventions in the Karolinska Medical Records	32	12	139 (until August 2014)
Total numbers of Bronchoscopies registered in the Karolinska Medical Records	n/a	n/a	4.199 (until September 2014)