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Endoscopic Bronchopleural Fistula Repair Using Autologous Fat Graft / Marchioni, Alessandro; Mattioli, Francesco; Tonelli, Roberto; Andreani, Alessandro; Cappiello, Gaia Francesca; Serafini, Edoardo; Stefani, Alessandro; Marchioni, Daniele; Clini, Enrico. - In: THE ANNALS OF THORACIC SURGERY. - ISSN 1552-6259. - 114:5(2022), pp. e393-e396. [10.1016/j.athoracsur.2022.02.014]

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16/08/2024 14:35

(Article begins on next page)

# The Annals of Thoracic Surgery

## Endoscopic bronchopleural fistula repair using autologous fat graft

--Manuscript Draft--

<b>Manuscript Number:</b>	ANNALS-22-00305
<b>Article Type:</b>	How to Do It
<b>Section/Category:</b>	General Thoracic
<b>Keywords:</b>	Bronchopleural fistula; Bronchial endoscopy; autologous fat implantation
<b>Manuscript Classifications:</b>	Bronchoscopy/bronchus; Fistula; Stem cells
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<b>Manuscript Region of Origin:</b>	ITALY
<b>Abstract:</b>	Bronchopleural fistula represents a not rare catastrophic complication of pulmonary resection with high mortality rates. While surgical treatments of BPF are often technically difficult and can only be tolerated by a limited number of patients, less invasive endoscopic approaches showed variable success rates, mainly related to the size of the fistula. With this report, we describe for the first time the successful treatment of large BPF by means of endoscopic autologous fat implantation and we discuss the surgical technical details of the procedure.

# 1 Endoscopic bronchopleural fistula repair using autologous fat graft

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3 Running head: lipofilling for bronchopleural fistula

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17 Words count: 1499

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## 31 Abstract

32 Bronchopleural fistula represents a not rare catastrophic complication of pulmonary resection with  
33 high mortality rates. While surgical treatments of BPF are often technically difficult and can only be  
34 tolerated by a limited number of patients, less invasive endoscopic approaches showed variable  
35 success rates, mainly related to the size of the fistula. With this report, we describe for the first time  
36 the successful treatment of large BPF by means of endoscopic autologous fat implantation and we  
37 discuss the surgical technical details of the procedure.

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## 40 **Introduction**

41 Bronchopleural fistula (BPF) occurs in 4.5-20% of patients who underwent pneumonectomy and in  
42 0.5-15% of patients after lobectomy, thus constituting a catastrophic complication burdened by  
43 high mortality rates(1). Open surgical approaches to BPF are often technically difficult and can only  
44 be tolerated by a limited number of patients(2). Less invasive endoscopic techniques showed  
45 variable success rates (30-80%), being these related to the size and the timely diagnosis of the  
46 fistula(3). Autologous fat grafting (AFG) is used as a successful approach to restore deficient tissue  
47 in esthetic and reconstructive surgery(4). Fat tissue is a source of mesenchymal stem cells with  
48 regenerative potential(4,5). Endoscopic injection of adipose tissue-derived stromal cells (ASC),  
49 derived by autologous fat (lipofilling), was reported effective in fistulas smaller than 6 mm(5). Also,  
50 grafting with fragmented pieces of fat harvested from the anterior abdominal wall, is used for  
51 reconstructing skull base defects, and preventing cerebrospinal fluid leakage, even in cases of  
52 extended dural defects and via endoscopic trans-nasal approach(6). In this report, we describe the  
53 use of abdominal free fat to BPF repair via endoscopic approach in two patients suffering from  
54 large fistulas in whom a previous endoscopic treatment had failed, and we discuss the surgical  
55 technical details of the procedure.

56

## 57 **Technique**

58 A 77-years-old Caucasian male affected by non-small lung carcinoma underwent a right inferior  
59 lobectomy complicated with a small BPF at the lateral segment of the middle lobar bronchus and a  
60 large BPF (7mm) in the bronchial stump. Similarly, a 72-years-old Caucasian female developed  
61 recurrent large fistula (7mm) located at the surgical bronchial stump one year after right lower lobe  
62 for non-small lung cancer. Both patients presented BPF recurrence despite endobronchial valve  
63 positioning and the insertion of expandable polyvinyl alcohol and cyanoacrylate glue. They were  
64 thus candidate to endoscopic autologous fat implantation to restore deficient tissue. Written  
65 informed consent regarding publication was obtained from both patients.

### 66 *Graft harvesting*

67 A curvilinear, periumbilical incision was used to expose the abdominal fat pad. Valid hemostasis  
68 was obtained with electrocautery at surgical site. Care was taken to limit the dissection to the  
69 superficial section of the abdominal muscular fascia. To avoid errors in volume estimation, the fat  
70 harvest for grafting was 30-40% higher than the estimated amount needed to fill BPF size.

### 71 *Graft placement*

72 In the same surgical session, endoscopic interventional procedures were performed with a Dumon  
73 rigid bronchoscope (Efer Medical, La Ciotat, Cedex, France) under general anesthesia. After  
74 locating the BPF, the mucosa surrounding the lumen of the fistula was ablated with argon plasma  
75 coagulator (APC 50W) to obtain an inflammatory de-epithelized area suitable for receiving fat  
76 transplantation. The harvested abdominal fat wrapped in a thin strip of absorbable oxidized

77 regenerated cellulose (Tabotamp®; Ethicon, Johnson & Johnson, respectively Surgicel® as its  
78 brand name in the USA) was placed *en bloc* into the prepared area through endoscopic forceps.  
79 Particular attention was paid to check that the graft was well seated and immobilized, completely  
80 occupying the fistula with a graft fat part facing into the pleural side. High molecular weight  
81 hyaluronic acid (Hyalubrix, Fidia Farmaceutici S.p.A., Abano Terme, Padova, Italy) was injected  
82 into the submucosa upstream of the fistula at three separate points to obtain a stable swelling of  
83 the wall and subsequent closure and further stabilization of the graft into the BPF. Synthetic  
84 biodegradable cyanoacrylate glue (Glubran 2, GEM Srl, Viareggio, Italy) was injected in the  
85 transplanted area and into the plug to expand it and to create an elastic film in the bronchial side to  
86 guarantee strong adhesion of the fat graft to the surrounding tissue. Figure 1 and 2 summarize the  
87 different steps of the surgical procedure used to achieve BPF closure.  
88 For both patients air leak stopped immediately after interventional bronchoscopy (Figure 3) and did  
89 not recur in the following 3 months.

90

#### 91 **Comment**

92 Despite initial observations showed that lipofilling might be effective in the treatment of medium-  
93 size BPF, the use of a piece of abdominal free fat to replace a large bronchial defect due to BPF  
94 had not been described yet(5). Subcutaneous fat tissue consists predominantly of adipocytes,  
95 ASCs, connective tissue, and it is rich in capillary network. Grafted non-vascularized adipose tissue  
96 is placed under ischemia and requires a suitable recipient bed which allows nutrient diffusion from  
97 surrounding host tissue until revascularization occurs(7). Large pieces of devascularized fat  
98 undergo partial necrosis and volume loss up to 50% before revascularization is established,  
99 limiting the size of the defect to fix through AFG. Among cellular components of adipose tissue,  
100 ASCs can survive in severe hypoxic environment even for 3 days contributing to the repairing  
101 process and to angiogenesis. In our two cases, intervention success could depend on several  
102 factors. First, both patients underwent a previous ineffective endoscopic treatment, which usually  
103 results in an inflammatory response of the stump. Second, the use of argon plasma coagulator to  
104 scarify the fistula could have amplified tissue inflammation and neovascularization from the  
105 surrounding tissue. Finally, the use of synthetic glue and hyaluronic acid are critical factors to  
106 maintain fat graft at the fistula site. Despite the success reported in our two cases, the gradual  
107 decrease in graft size over time because of necrosis and apoptosis of fat cells represents a  
108 limitation(7). Such atrophy can potentially re-open a successfully occluded fistula. However, both  
109 patients kept fistula closure on endoscopic and radiographic evaluation performed 3 months after  
110 surgery. In conclusion, we described for the first time the successful treatment of large BPF  
111 through autologous fat implantation, discussing the technical peculiarities and the limits of the  
112 procedure. Further studies are needed to confirm this preliminary report.

113

114 **Acknowledgments and disclosures**

115 None.

116

117 **Figure legend**

118

119 **Figure 1. AFG for BPF treatment**

120 **A:** Periumbilical incision and exposition of abdominal fat pad for fat harvest. **B:** Fat graft size is  
121 chosen based on the size of the fistula.

122

123 **Figure 2. Surgical endoscopic technique**

124 **A:** BPF in the bronchial stump. **B:** After ablation of the margins of the BPF with argon plasma  
125 coagulator, fat graft is placed into the fistula through endoscopic forceps. **C:** Using a laser holder  
126 wand, the fat graft is pushed into the fistula until it is immobilized. After this procedure, high  
127 molecular weight hyaluronic acid was injected into the submucosa upstream of the fistula to obtain  
128 further stabilization of the graft into the BPF. **D:** Synthetic biodegradable cyanoacrylate glue was  
129 injected in the transplanted area and into the plug, achieving strong adhesion of the fat graft to the  
130 surrounding tissue

131

132 **Figure 3. Upper part: CT scan of patient 1. A:** CT scan showing large right hydropneumothorax  
133 due to BPF in the bronchial stump of right inferior lobectomy. **B:** CT scan two weeks after  
134 endoscopic treatment showing resolution of hydropneumothorax. **Lower part: CT scan of patient**  
135 **2.** CT scan showing BPF in the bronchial stump of right inferior lobectomy. **D:** CT scan two months  
136 after endoscopic treatment showing persistent closure of the fistula

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