

# Anterograde Injection of Alteplase Salvages Deep Inferior Epigastric Perforator Flap in Reconstructive Breast Surgery

Julia M. Wimbauer, MD  
 Klemens M. Heinrich, MD  
 Karl Schwaiger, MD  
 Peter Pumberger, MD  
 Fabian Koeninger, MD  
 Gottfried Wechselberger, MD,  
 MSc  
 Elisabeth Russe, MD

**Summary:** The DIEP flap is currently considered the gold standard for autologous reconstructive breast surgery. Postoperative flap failure due to microvascular post-anastomotic thrombotic occlusion is a rare but severe complication. Alteplase, a thrombolytic agent typically used in the setting of an ischemic stroke, myocardial infarction, or pulmonary embolism, has also been injected into the microcirculation of flaps as a rescue procedure due to imminent flap loss. The purpose of this article is to provide an overview and detailed guidance for such a thrombolytic procedure due to suspected thrombotic microsurgical failure in free flap surgery. We report the case of a 43-year-old woman who underwent unilateral breast reconstruction with a DIEP flap at our department. Approximately 12 hours postoperatively, an arterial inflow problem was suspected and revision surgery was performed. Peripheral flap perfusion remained absent without an obvious cause and distal thrombosis was assumed to be present. Therefore, alteplase was gradually injected into the arterial pedicle in the anterograde direction just distal to the anastomosis while clamping the artery proximally. About 3 hours after selective flap thrombolysis, microcirculation of the flap was successfully restored without complications. Anterograde injection of alteplase can successfully salvage a free flap. To our knowledge, evidence for optimal dosing and delivery of alteplase for the treatment of thrombosed DIEP flaps has not been published to date. Our approach presents a therapeutic option that both maximizes alteplase concentration in the flap and minimizes the dosage required for flap salvage to significantly reduce systemic adverse effects. (*Plast Reconstr Surg Glob Open* 2022;10:e4415; doi: 10.1097/GOX.0000000000004415; Published online 20 June 2022.)

The use of deep inferior epigastric perforator (DIEP) flap for free-tissue transfer has become the gold standard procedure for autologous breast reconstruction surgery. However, postoperative flap failure due to microvascular postanastomotic thrombotic occlusion is a rare but severe complication that requires prompt intervention.<sup>1</sup> Complications of the microvascular anastomoses,

such as arterial or venous thrombosis, often cause irreversible damage to the microcirculation; therefore, adequate treatment is essential to increase flap salvage rates.<sup>2-4</sup> If exploration and revision of the anastomosis is inadequate for flap salvage, often pharmacologic assistance in the management of a failing flap is needed. We report on the successful salvage of a compromised DIEP flap with anterograde injection of alteplase, the recombinant tissue plasminogen activator (rt-PA), into the arterial pedicle.

*From the Department of Plastic, Aesthetic and Reconstructive Surgery, Hospital of St. John of God Salzburg, Paracelsus Medical University Salzburg, Salzburg, Austria.*

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## CASE REPORT

A 43-year-old woman with a history of breast cancer of the left breast presented at our hospital and asked for autologous breast reconstruction. The decision was made to perform a DIEP flap 1 year after uneventful follow-up.

A single venous anastomosis was performed with a 2.0-mm coupler between the inferior epigastric vein and the internal mammary vein at the level of the fourth rib. Microvascular anastomosis between the deep inferior epigastric artery and the internal mammary artery with a

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noticeable difference in the caliber was performed with 8-0 nylon. Intraoperatively, 40mg intravenous bolus of heparin was given. Postoperatively, our thrombosis prophylaxis regimen included subcutaneous heparin, 20mg in the morning and 40mg in the evening.

**Clinical Findings**

Approximately 12 hours postoperatively, an arterial inflow problem was suspected and revision surgery was performed. Despite a patent arterial anastomosis was confirmed by Doppler sonography and probing, peripheral flap perfusion remained absent without an obvious cause.

Inspection of the vascular pedicles revealed no twisting, kinking, and external compression of the pedicle could be excluded. Both Doppler sonography and milking test were performed to confirm patency of the donor artery and vein, anastomosis, and the recipient artery and vein. Distal thrombosis was assumed to be present, when peripheral flap perfusion remained absent without an obvious cause.

**Therapeutic Focus and Assessment**

Therefore, in an attempt to salvage the flap, a 2-ml bolus of alteplase was gradually injected into the arterial pedicle in antegrade direction just distal to the anastomosis without removing stitches to prevent loss of solution. Additionally, the artery and vein were clamped proximally for about 8 minutes (Fig. 1). This allowed the solution to stand for that period in the flap, before reestablishment of arterial blood flow. Also, a small area of the flap was deepithelialized for monitoring purposes (Fig. 2).

**Follow-up and Outcomes**

About 3 hours after selective flap thrombolysis, microcirculation of the flap was successfully restored. Postoperatively, normal wound healing was noticed. At a 3-month follow-up, the salvaged flap was soft throughout;

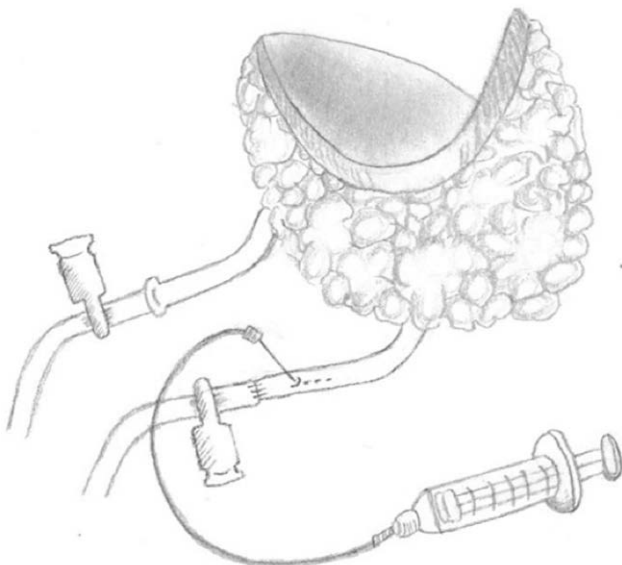


**Fig. 2.** Flap after revision surgery with a small area deepithelialized for monitoring purposes.

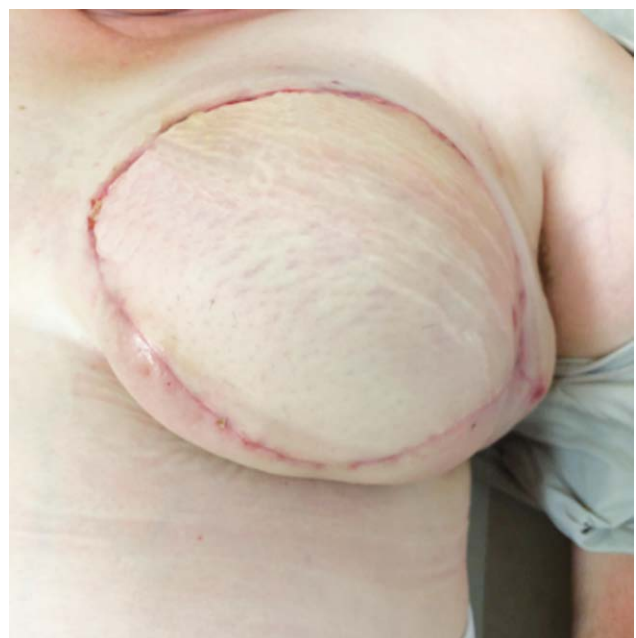
no other complications including fat necrosis or hemorrhage occurred (Fig. 3).

**DISCUSSION**

Although thrombolytic agents have been used in a few clinical studies and most authors recommend the local use of thrombolytic agents,<sup>5-9</sup> pharmacological thrombolysis has been overlooked by many reconstructive microsurgeons. However, there often exists the fear of systemic complications such as bleeding tendency and hypertension.



**Fig. 1.** Schematic of anterograde injection of alteplase.



**Fig. 3.** Flap after a 3-month follow-up.

The use of thrombolytic agents such as alteplase, urokinase, streptokinase, and acylated-plasminogen-streptokinase-activator-complex are the most commonly used thrombolytic drugs which have been shown to be effective for flap salvage in animal studies.<sup>10–12</sup> However, there have also been a few clinical studies of thrombolytic therapy in free-tissue transfer for flap salvage in clinical setting reported.<sup>5–9</sup> There are only some differences between the individual thrombolytic agents.

Alteplase has been widely used in the treatment of myocardial infarction, pulmonary embolism, or ischemic stroke and is also the most clinically used thrombolytic agent to salvage compromised flaps.<sup>13,14</sup>

In our case, alteplase was used because of its clinical availability and our familiarity with its actions. Establishing the optimal rt-PA doses for treating microvascular thrombosis in free flaps is difficult, as ideal doses and delivery procedures have not been reported so far. In our case the bolus of 2 ml of alteplase was based on the weight of the flap (1950 g), as we followed the guidelines for the acute stroke therapy which recommend 0.9 mg/kg for optimal lysis of thrombi when infusing systemically. Higher concentrations may increase the risk of hemorrhage without increasing the efficacy. Baumer et al reported in their in vitro thrombolysis study a dose dependent decrease in thrombus weight induced by rt-PA. Based on these findings, it is recommended to administer no more than 1 mg/kg rt-PA for optimal lysis of thrombi when infusing systemically.<sup>15–17</sup>

Nevertheless, our current procedure maximizes the rt-PA gradient in the flap, minimizes the total dose required and ensures prevention of systemic spread or systemic side effects.

We applied a vessel clamp on the artery, as well as on the vein distal to the anastomosis, to allow the solution to stand for that period in the flap, before reestablishment of arterial blood flow. Without clamping the artery, increased pressure in the flap and recipient artery may cause backflow, potentially causing systemic spread of alteplase. Even the blood continually flowing into the flap may reduce the alteplase gradient in the flap and thus additional doses of alteplase might be required without clamping.

## CONCLUSIONS

Our approach presents a therapeutic option that both maximizes alteplase concentration in the flap and minimizes the dosage required for flap salvage. Therefore, it has the potential to significantly reduce adverse effects associated with systemic administration of thrombolytic agents.

For the treatment of thrombosis in free flap surgery, guidelines on optimal dosing regimens or application periods of thrombolytic agents are still not available. To our knowledge, evidence for optimal dosing and delivery of alteplase for the treatment of thrombosed DIEP flaps has not been published to date. We can only follow existing hospital guidelines and protocols on thrombolytic therapy when choosing a thrombolytic agent. There are prospective randomized studies needed concerning their indications, dosages, and methods of administration, as well as their efficacy and safety.

## ETHICAL APPROVAL STATEMENT

The study was performed in accordance with the principles outlined in the Declaration of Helsinki, and informed consent for participation was obtained and registered.

*Julia M. Wimbauer, MD*

Hospital of St. John of God (Barmherzige Brüder) Salzburg  
Department of Plastic, Aesthetic and Reconstructive Surgery  
Paracelsus Medical University (PMU) Salzburg  
Kajetanerplatz 1, 5020 Salzburg, Austria  
E-mail: julia\_wimbauer@hotmail.com

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