

# Surgical approaches to autologous limbal stem cell transplantation (LSCT) following severe corneal chemical burns

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## Abstract

Chemical injury of the conjunctiva and cornea are true ocular emergencies and require immediate intervention. They can produce severe and extensive eye damage including limbal stem cell deficiency (LSCD), which can lead to loss of vision. LSCD can be surgically treated through autologous limbal stem cell transplantation (LSCT). Autologous LSCT can be performed through cultivated limbal epithelial transplantation (CLET) or by direct grafting of limbal epithelial cells through conjunctival-limbal autografting (CLAU) or simple limbal epithelial transplantation (SLET). In this review we provide an overview of each surgical approach. CLET allows a large graft implantation in the receiving eye while saving donor cells. Its success rate is higher with an increased number of transplanted stem cells and failures tend to happen within the first year. CLAU is achieved by directly transplanting autologous limbal stem cells from the patient's healthy eye, reducing the risk of immune rejection. It represents a risk for the donor eye as the removal of stem cells from the contralateral eye may present risks of LSCD. SLET consists of direct implantation of donor stem cells on an amniotic membrane, thus bypassing the need for ex-vivo expansion. Combinations of CLAU and SLET within a single procedure have also been successfully used. Autologous LSCT is an effective surgical management technique for unilateral LSCD. Depending on the patient history and status of the donor eye CLET, CLAU or SLET (incl. the combination of mini-CLAU and SLET) can be used to restore long-term function and protect from visual impairment.

**Keywords:** limbal graft, limbal epithelial transplantation, simple limbal epithelial transplantation (SLET), conjunctival-limbal autologous transplantation (CLAU), cultivated limbal epithelial transplantation (CLET)

## Introduction

Chemical injury of the conjunctiva and cornea are true ocular emergencies and require immediate intervention as they can produce severe and extensive damage to the ocular surface and anterior segment including limbal stem cell deficiency (LSCD) (1). Untreated LSCD in turn causes pain, decreased vision, and

recurrent epithelial erosions leading to infection and loss of vision. LSCD can be surgically treated through autologous limbal stem cell transplantation (LSCT). Three different surgical approaches have evolved using the healthy contralateral limbus namely: cultivated limbal epithelial transplantation (CLET), conjunctival-limbal autografting (CLAU) and simple limbal epithelial transplantation (SLET). We provide an overview of each surgical approach respectively, addressing their clinical safety and efficacy profiles.

## Management of Chemical Injuries

Management of chemical injuries depends on the stage of presentation. In the acute stage, treatment goals are re-epithelialization, inflammation and intraocular pressure control (1). Amniotic membrane corneal transplantation (AMT) represent the mainstay of therapy to induce short-term epithelialization, but lack any long-term benefits, especially in terms of improving visual acuity (2)(3).

In case of extensive corneal conjunctivalization and a unilateral LSCD, autologous LSCT have been described using various techniques (4). Contrary to allogenic transplantation, autologous transplantation techniques avoid the risk of graft rejection and prolonged immunosuppression (5). Autologous LSCT can be performed either after cultivation on a biological membrane (CLET) or by direct grafting of limbal epithelial cells (CLAU and SLET).

### CLET

To minimize loss of donor limbal tissue and the possibility of inducing LSCD in the donor eye, or in bilateral LSCD, CLET uses ex-vivo cultivated limbal epithelial cells for transplantation (6) (7). First introduced by Pellegrini et al, it consists of harvesting 1 or 2 mm of healthy limbus from the contralateral eye and expanding it in a laboratory (6). Different culture medias and techniques have been described with good results (8)(9)(10). It allows a larger graft implantation in the receiving eye while saving donor cells in case of a second intervention. CLET has the benefit of requiring less donor tissue and thus being safer for donor eyes (8)(11). In a review of outcomes of cultured limbal epithelial cell therapy published from 1997 to 2011 with data

from 583 patients, the overall success rate was 76% (11). However, the success rate of a transplant is significantly higher with an increased number of transplanted stem cells and failures tend to happen within the first year (12).

### Direct grafting of limbal epithelial cells (CLAU & SLET)

Direct grafting of limbal epithelial cells through CLAU and SLET, have better anatomical and functional success rates in comparison to CLET (13). A prospective study comparing SLET vs CLAU done by R. Arora et al. concluded that both procedures were equally effective, providing stable results (14).

#### CLAU

CLAU was described in 1986 by Dr. K. Kenyon and Dr. G. Tseng as the first limbal transplantation describing a sectorial limbal harvesting from the donor eye (15). The procedure is achieved by directly transplanting autologous limbal stem cells from the patient's healthy eye, hence reducing the risk of immune rejection, and with no need for systemic immunosuppression. However, this procedure represents a risk for the donor eye. Indeed, the removal of stem cells from the contralateral eye may present risks LSCD in the donor eye. The risk is low when less than four to six clock hours of limbal tissue and a moderate amount of conjunctiva are removed (16). In their recent long-term follow-up study where they report excellent anatomical and functional results, Eslani et al recommend harvesting at most 5 clock hours to avoid LSCD in the donor eye (17).

#### SLET

First described in 2012, SLET consists of direct implantation of donor stem cells on an amniotic membrane, placed on the ocular surface of the recipient, thus bypassing the need for ex-vivo expansion (18). It minimizes donor limbal tissue loss and the possibility of inducing LSCD in the donor eye. SLET is hence a reproducible, single stage technique that is more conservative for the donor eye, allowing harvesting a smaller limbal graft than CLAU. Optimization of the ocular surface including rapid resolution of inflammation is important to give the best chance for successful outcome. The most common complication of SLET is the focal recurrence of LSCD, which can limit visual recovery (19). Vazirani et al. suggested that repeat SLET can be of benefit (19). During the post-operative period, displacement of the graft is common when a posterior postoperative membrane bleeding occurs. Clinical factors known to be associated with poor outcomes of the procedure are acid injury, severe symblepharon, inflammation, combination with keratoplasty and postoperative loss of explants (18)(19)(20)(21).

### Combining SLET and mini-CLAU

In situations with a high risk of SLET failure due to focal pannus recurrence because of pseudo-ptyerygium or a symblepharon, a customized SLET combined with a mini-CLAU could be envisaged (21)(22). It is important to balance this combination against an increased risk to the donor eye of losing

a significant amount of limbal tissue. The use of the mini-CLAU technique limits this risk.

### Conclusion

Autologous LCST emerges as an effective surgical management technique for unilateral LCSD. Depending on the patient history and status of the donor eye CLET, CLAU or SLET (incl. the combination of mini-CLAU and SLET) can be used to restore long term function and protect from visual impairment.

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