Composite Tissue Allografts for Burn Injuries

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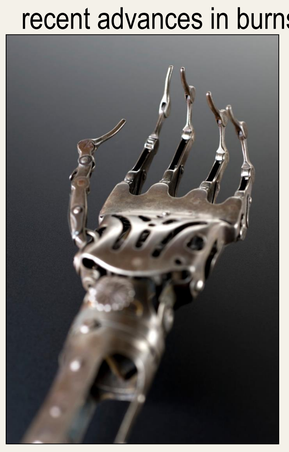
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Introduction

Composite tissue allotransplantation (CTAs) or vascularized composite allografts (VCAs) are a procedure used to address the problems surrounding burn injuries. In recent years, prosthetics have advanced to overcome the problems preventing the widespread use of CTAs. Recent advances in transplantology and plastic surgery are improving the quality of these allografts. Facial and hand transplants have been performed and the majority of successful VCAs.

Aims

To review the continued viability of CTAs as an advanced reconstructive method for the treatment of burn injuries in light of recent advances in burns and transplantation surgery.



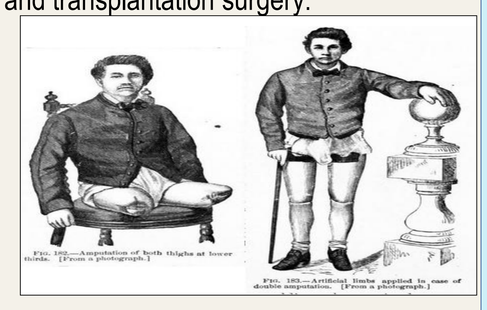




Fig 1: Older prosthetics and a modern osseointegrated prosthetic

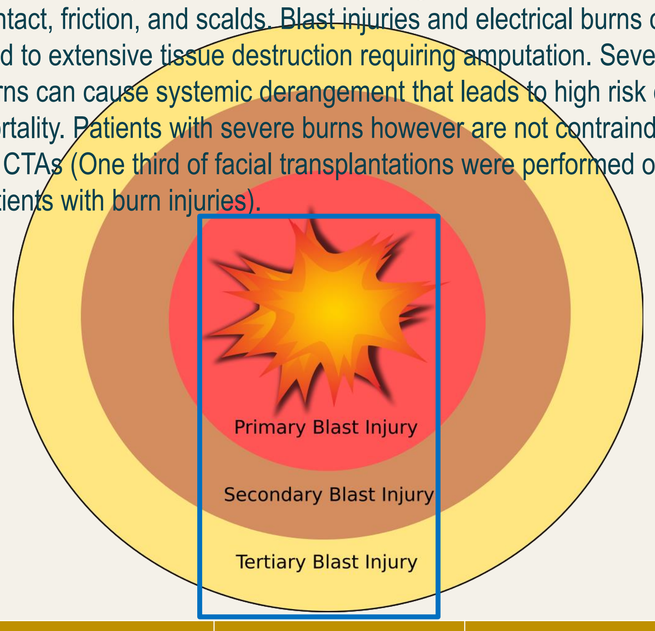
Methods

A Pubmed search was conducted to access the Medline database using the terms “burns”, “vascularized composite allografts” and “composite tissue allotransplantation”.

Epidemiology and Aetiopathogenesis

Burn Injuries

Burns are a form of mutilating injury to tissue caused by thermal heat. There are many causes of burns including flame, electric, flash, contact, friction, and scalds. Blast injuries and electrical burns can lead to extensive tissue destruction requiring amputation. Severe burns can cause systemic derangement that leads to high risk of mortality. Patients with severe burns however are not contraindicated for CTAs (One third of facial transplantations were performed on patients with burn injuries).



Type	Mechanism	Examples
Primary	Direct blast wave injuries	Tympanic membrane rupture, blast lung
Secondary	Injury due to shrapnel impact	Penetrating injuries
Tertiary	Injury due to bodily displacement	Fractures, traumatic amputations
Quarternary	Miscellanous	Burns, inhalational injuries

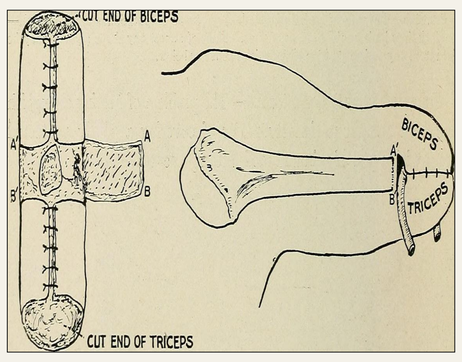
Different types of Blast Injury in the Blast Radius

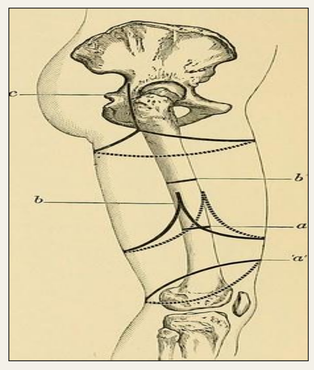
Blast Injuries

Injury due to blast trauma has seen a recent uptick in incidence. These are most commonly caused by Improvised Explosive Devices (IEDs), in the leg and forearm producing complex injuries with progressive damage across structures and compartments of the area afflicted. Fireworks may also cause these injuries.

Current

The current gold standard to complex limb reconstruction is an initial orthoplastic approach. This will help in managing extensive limb damage with early debridement, reconstruction, and soft tissue cover (Wordsworth, MacIver et al. 2014)(Lerman, Kovach et al. 2011)





Illustrations of traditional methods of amputation

Composite Tissue Allografts

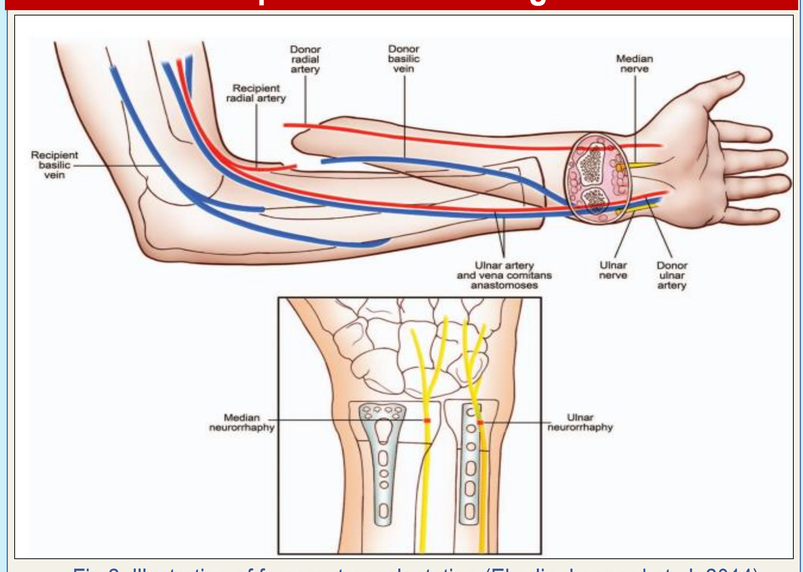


Fig 2: Illustration of forearm transplantation (Eberlin, Leonard et al. 2014)

Immune Issues in VCA are caused by **Sensitisation**

1) MHC II and Langerhans cells of skin-containing VCAs result in increased immunogenicity compared to organ transplants.
2) Triple therapy (mycophenolate mofetil, tacrolimus, methylprednisolone) and other adjuncts are commonly used in VCA with a high rate of acute rejection within the first year due to cellular immunity rather than antibody mediated rejection seen in organ transplants.(Klein, Schanz et al. 2016)
3) Immunosuppressant toxicity remains a problem
4) Multiple VCAs are associated with high mortality due to metabolic failure, infection, cardiac arrest, and organ failure.

In burns, sensitization is increased by blood transfusions, dermal allografts, and unknown factors resulting in a rise of HLA sensitisation in polytrauma (Xiao, Mindrinos et al. 2011).

Improvements

Early transplantation has been proposed to reduce the risk of rejection and provide soft tissue cover. Restrictive transfusion protocols agree with recent trauma guidelines

VCAs are complex and the most recent advances in transplantation medicine and reconstructive surgery can optimise outcomes. These methods and precautions include.

1) Sentinel Flaps

Used to indicate graft failure

2) Preconditioning

Hypoxia-inducing factors (and IFN-γ donor preconditioning can delay VCA rejection.

3) Early Transplantation

Blood transfusion and cadaveric dermal allografts increase VCA rejection in burn patients (Press, Lee et al. 2017)..

4) Tolerance

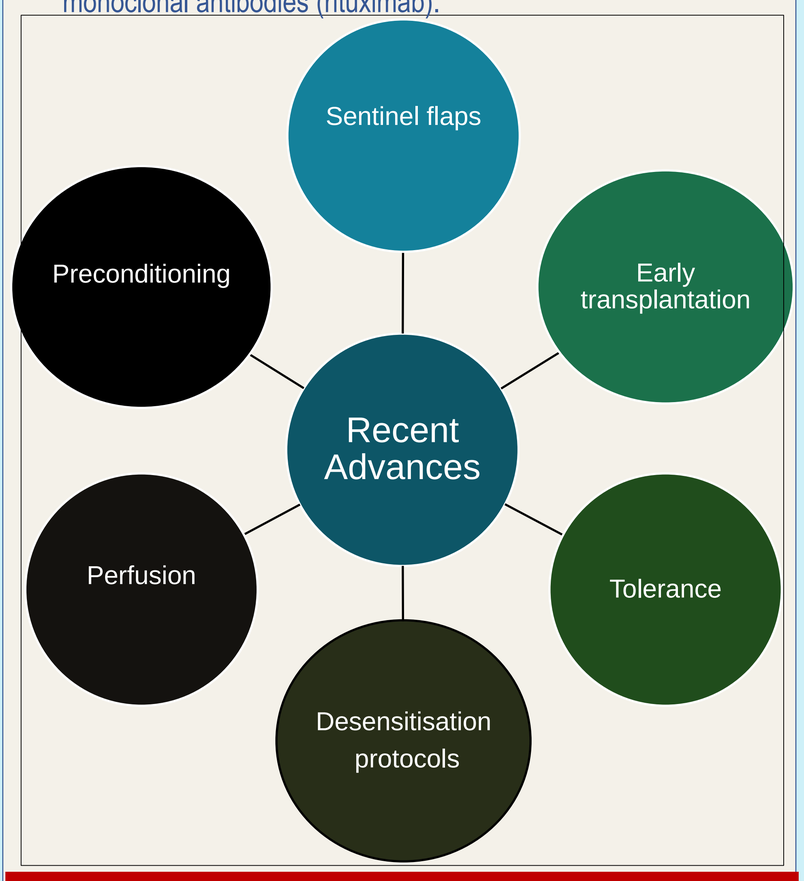
T-regulator cell therapy and bone marrow transplants can be attempted to induce chimerism and graft tolerance

5) Perfusion

Modern perfusion has shown increased warm ischaemic time of solid organs. Extracorporeal devices are proposed for VCAs

6) Desensitisation

Plasma exchange, immunoadsorption, IVIG, mTOR inhibitors (rapamycin), pulsed steroids, calcineurin inhibitors (tacrolimus), anti-thymocyte globulin and monoclonal antibodies (rituximab).



Monitoring

Skin is highly allogenic (Robbins, Wordsworth et al. 2019). However, imaging modalities like Laser Doppler Imaging (as used in burns), Magnetic Resonance Imaging, and other blood markers may allow better monitoring of rejection.

Banff Classification for VCAs with Skin

Grade of Rejection	Perivascular Inflammation	Epidermal Involvement
0 (no)	None	None
I (mild)	Mild	None
II (moderate)	Moderate	Mild (Oedema or lymphocytic exocytosis)
III (severe)	Dense	Apoptosis, dyskeratosis, keratinolysis
IV (acute necrosis)	Frank epidermal or adnexal necrosis	

Conclusion

Vascularised tissue allotransplantation remains a viable approach to devastating injuries caused by burns. Research into this field is extensive but still more is required to improve the viability of VCAs at 1 year. The procedures are very complex. The outcomes are currently variable but can be optimised to last longer with advances in the field making them suitable for burn patients.

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