Composite Tissue Allotransplantation for Burn and Blast Injuries

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Introduction

Burn injuries can be reconstructed using Vascularised Composite Allografts (VCAs) in Composite Tissue Allotransplantations (CTAs). Recent advances in transplantology and plastic surgery have improved the survival and quality of CTAs, which are competitive alternatives to prosthetics.

Facial and hand transplants were the first breakthroughs in CTA.

Aims

To review recent advances in plastic and transplant surgery in CTAs used in burns reconstruction.

Methods

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

Epidemiology and Aetiopathogenesis

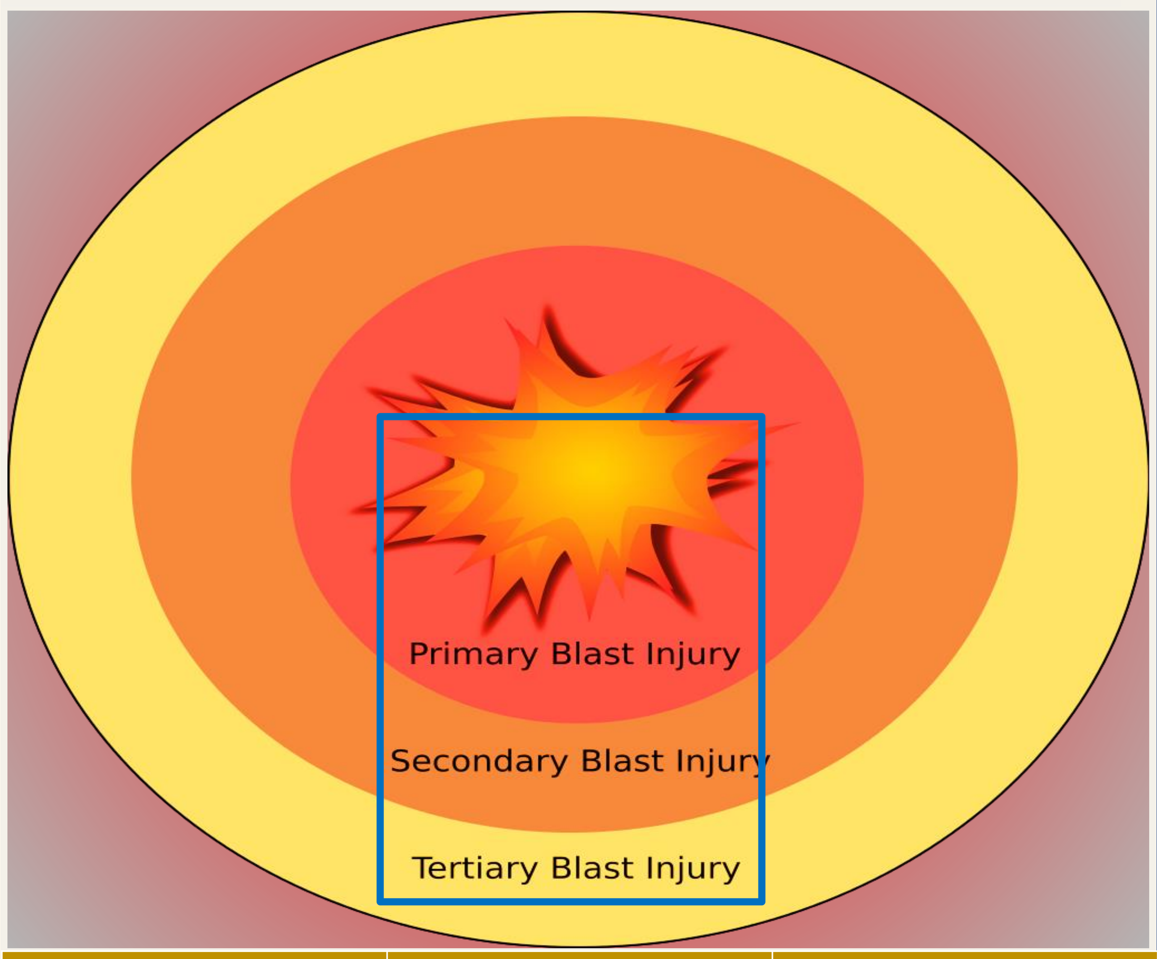
Burn Injuries

Burns are a form of mutilating injury to tissue caused by thermal energy. 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).

Blast-related Burn Injuries

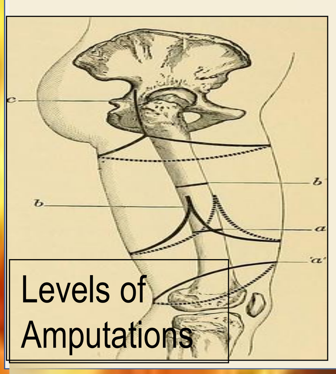
The incidence of blast injuries has increased, especially due to Improvised Explosive Devices (IEDs). Due to the configuration of present day armour, complex injuries are especially seen in the exposed limbs. Fireworks and electrical arc flashes also cause these injuries.



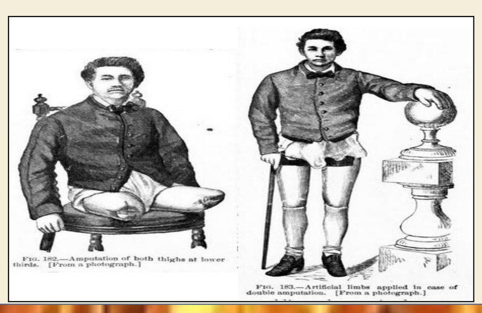
Type	Mechanism	Examples
Quarternary	Thermal Radiant	Fireball – Fatal Flash burns
Quinary	Conflagration	

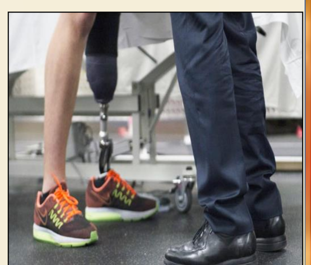
Reconstructive Options

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)



Levels of Amputations



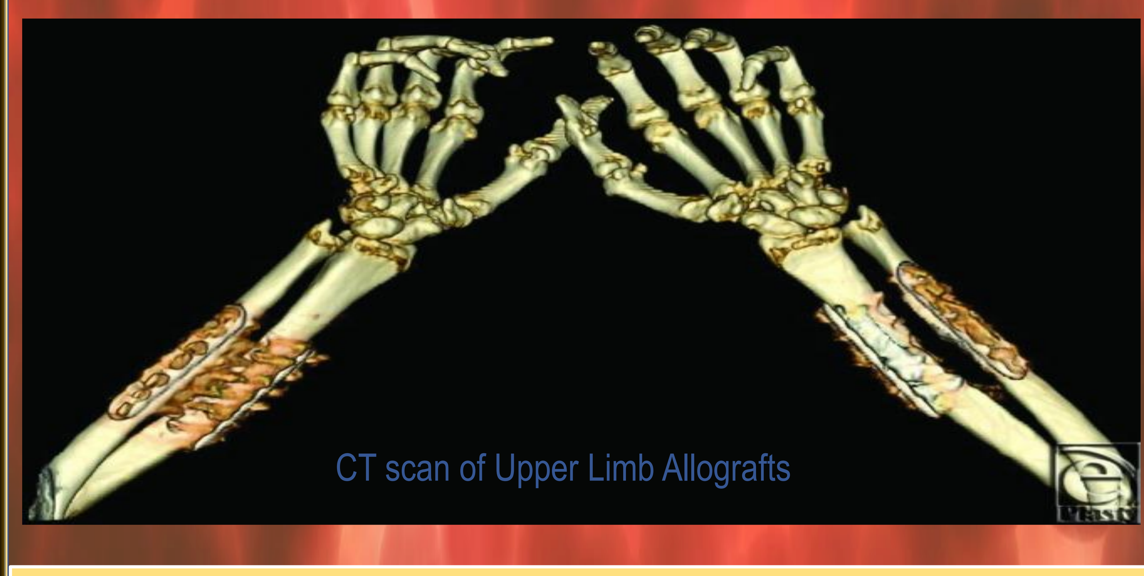


Osseointegrated prosthetic

Upper Limb Prosthetics

Fig 3: Advances in Upper Limb Reconstruction (Kalantar-Hormozi et al.2013)

Composite Tissue Allotransplantation



CT scan of Upper Limb Allografts

Alloimmune Responses in CTAs

MHC Class II-expressing Langerhans cells of skin-containing CTAs are immunogenic and are more abundant compared to solid organ transplants

Immunosuppression toxicity remains a problem

Triple therapy (mycophenolate mofetil, tacrolimus, methylprednisolone) commonly used in CTA has a high rate of acute rejection from cellular immunity rather than antibody mediated rejection seen in organ transplants.(Klein, Schanz et al. 2016)

Multiple CTAs are associated with increased mortality

Sensitisation is increased by blood transfusion, dermal allografts and unknown factors resulting in a rise of HLA sensitisation in polytrauma (Xiao, Mindrinos et al. 2011

Functional Assessment Post- Transplant

Composite Tissue Allografts in Upper Limbs (Salminger et al., 2016)

Improvements in Allotransplantation

Early CTA for early definitive reconstruction is recommended to reduce the risk of rejection and provide soft tissue cover. Restrictive transfusion protocols agree with recent trauma guidelines and reduce sensitisation.

Recommendations

Pre – transplant (Patient preparation)

Tolerance

T-regulator cell therapy can be attempted to induce graft tolerance (Kawai, Uchiyama et al. 2018)

Graft Priming

Preconditioning

Mechanical or pharmacological ischaemic preconditioning (Akhtar, Sutherland et al. 2014) can delay CTA rejection by priming the transplant.

Graft Preservation

Perfusion

Modern perfusion has increased warm ischaemic time of solid organs. Extracorporeal devices are proposed for CTAs and glycerol preservation is preferred to cryopreservationon

Graft Monitoring

Sentinel Flaps

Free fasciocutaneous forearm flaps can be used as indicators of graft failure along with other biomarkers (exosomes)

Emergency VCA

Early Transplantation

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

Post – transplant (Treating rejection)

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 and blood markers may allow better monitoring of rejection than the traditional Banff classification.

Banff Classification for VCAs with Skin

Grade of Rejection	Perivascular Inflammation	Epidermal Involvement
0 (none)	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

Composite tissue allotransplantation remains a viable approach to devastating injuries caused by burns. Transplant advances can help plastic surgeons optimise long-term CTA outcomes in burn patients.

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