A Survey On The Usage Of Decellularized Tissues In Orthopedic Clinical Trials

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INTRODUCTION: Orthopaedic surgery requires grafts with sufficient mechanical strength. For this purpose, decellularized tissue is an available option that lacks the complications of autologous tissue. However, it is not widely used in orthopaedic surgeries. This study investigated clinical trials of the use of decellularized tissue grafts in orthopaedic surgery.

METHODS: Using the ClinicalTrials.gov (CTG) and the International Clinical Trials Registry Platform (ICTRP) databases, we comprehensively surveyed clinical trials of decellularized tissue use in orthopaedic surgeries registered before 1 September 2022. We evaluated the clinical results, tissue processing methods, and commercial availability of the identified products using academic literature databases and manufacturers' websites.

RESULTS: We initially identified 4,402 clinical trials, 27 of which were eligible for inclusion and analysis, including nine shoulder surgery trials, eight knee surgery trials, two ankle surgery trials, two hand surgery trials, and six peripheral nerve graft trials.(Figure 1) Nine of the trials were completed.(Table 1) Peracetic acid and gamma irradiation were frequently used for sterilization. We identified only one product that will be commercially available for use in knee surgery with significant mechanical load resistance.

DISCUSSION: Despite the demand for decellularized tissue, few decellularized tissue products are currently commercially available, particularly for the knee joint. To be viable in orthopaedic surgery, decellularized tissue must exhibit biocompatibility and mechanical strength, and these requirements are challenging for the clinical application of decellularized tissue. However, the variety of available decellularized products has recently increased. Therefore, decellularized grafts may become a promising option in orthopaedic surgery.

SIGNIFICANCE/CLINICAL RELEVANCE: Insights from our study provide valuable guidance for the improvement of decellularized tissue development processes. These findings contribute to the broader understanding of tissue engineering and regenerative medicine applications.

IMAGES AND TABLES

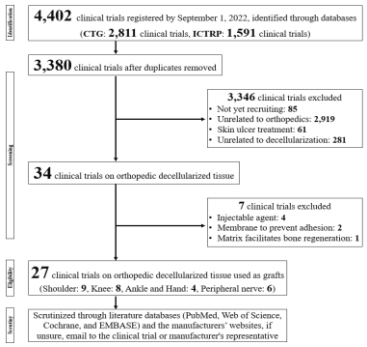

Figure 1: Flowchart of the clinical trial search process and the identification of decellularized products used in trials. We identified 4,402 trials initially and eventually reviewed a total of 27 trials: nine in the shoulder field, eight in the knee field, four in the ankle and hand field, and six in the peripheral nerve field. CTG, ClinicalTrials.gov; ICTRP, International Clinical Trials Registry Platform.

Table 1: Overview of nine completed orthopedic clinical trials using decellularized tissue

Condition	Clinical trial name	Product name	Source tissue	Country	Decellularization/Sterilization method
Rotator cuff tear	Use of graft jacket for rotator cuff repair	GRAFTJACKET allograft	Human dermis	USA	N/A; tissue underwent no general sterilization and freezing
Rotator cuff tear	Outcome evaluation of allograft scaffold augmentation for arthroscopic repair of full thickness of rotator cuff tear	CGDerm	Human dermis	South Korea	N/A
Rotator cuff tear	Clinical outcomes and structural integrity of arthroscopic superior capsular reconstruction using cryopreserved acellular dermal matrix with increased elasticity and thickness in patients with irreparable rotator cuff tear	CGDerm	Human dermis	South Korea	N/A
Rotator cuff tear	Acellular dermis in rotator cuff repair	N/A	Human dermis	UK	N/A
Rotator cuff tear	Allograft reconstruction of massive rotator cuff tears vs partial repair alone	Allopatch HD	Human dermis	Canada	N/A; harvested by sterile techniques; tissue underwent no general sterilization
CM arthritis of the thumb	Use of FlexHD as Post Trapeziectomy Spacer	FlexHD	Human dermis	USA	Non-ionic surfactant (Triton X-100)/ alcohol, peracetic acid
Peripheral nerve injury of upper limb	Human acellular nerve graft for repair of peripheral nerve defects: a prospective, multicentre clinical study	N/A	Human peripheral nerve	China	46 mM Triton X-100, 96 mM sodium deoxycholate; N/A
Peripheral nerve injury of upper limb	Human acellular nerve graft for repair of pure sensory nerve defects: a prospective, multicentre clinical study	N/A	Human peripheral nerve	China	46 mM Triton X-100, 96 mM sodium deoxycholate; N/A
Peripheral nerve injury of upper limb	Comparison of processed nerve allograft and collagen nerve cuffs for peripheral nerve repair (RECON)	Avance nerve graft	Human peripheral nerve	USA	50 mM phosphate +100 nM Na, 0.14% Triton X-200, 0.6 mM sulfobetaine-16/gamma irradiation

N/A, not available; CM, carpometacarpal