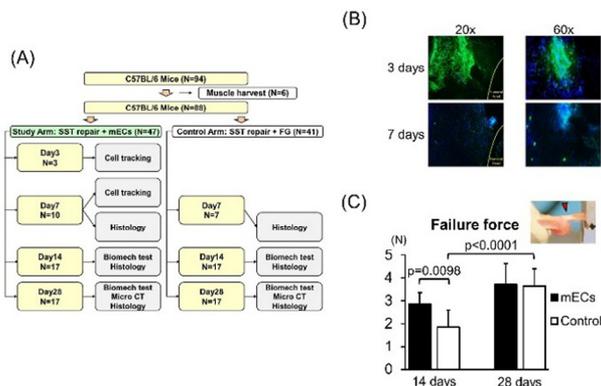


**Introduction:** Cell-based approaches are expected to improve tendon-to-bone healing in rotator cuff tendon injuries. Recently, a specialized population of endothelial cells which produce signaling molecules that stimulate the intrinsic stem cells in specific tissues have been identified and reported.<sup>4</sup> We hypothesized that endothelial cells from muscle tissue could stimulate and enhance the tendon-to-bone healing. The purpose of the present study is to evaluate the effects of the novel muscle-derived activated endothelial cells (mECs) implanted at the repair site in a murine rotator cuff repair model.

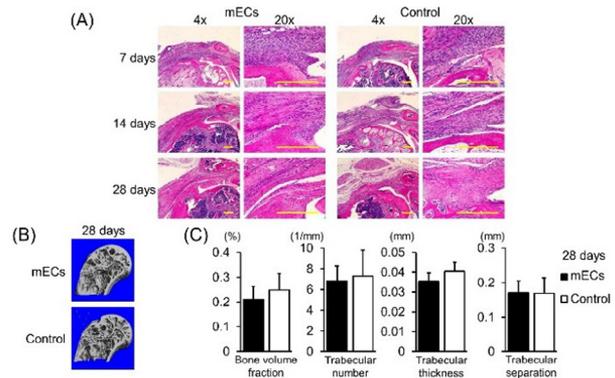
**Methods:** A total of ninety-four C57BL/6 mice were used in this study (Fig. 1, A). Six mice were euthanized and underwent muscle harvest, followed by endothelial cell isolation with subsequent transfection of adenoviral E4ORF1 and green fluorescent protein (GFP) labelling.<sup>2,3,5,7</sup> Eighty-eight C57BL/6 mice underwent unilateral microsurgical supraspinatus tendon (SST) detachment and repair with implantation of 100,000 mECs in a fibrin glue (FG) carrier vehicle (study group) or FG alone (control group). Three mice each were euthanized at 3 and 7 days after the surgery in the study group to check the cell viability and localization using fluorescent microscopy. The other mice were euthanized at 7, 14, and 28 days and used for biomechanical test, histological evaluations (hematoxylin-eosin, Alcian blue, and picosirius red), immunohistochemical staining (factor VIII) and micro computed tomography (μCT) analysis.<sup>1</sup> Statistical analysis was done using T-test and 2-way ANOVA with post-hoc Tukey's test. The significance limit was set at  $P = .05$ .

**Results:** Cell tracking (Fig. 1, B): There were GFP positive mECs at the repair site of SST at day #3 in the study group. Biomechanical testing (Fig. 1, C): The failure force in the study group was significantly higher than that of the control groups at day #14 (2.87 vs 1.86 N,  $P = .0098$ ). Histology (Fig. 2, A): Increased cellularity and vascular tissue formation at the repair site of SST were observed in the study group at day #7. Improved continuity of the repaired SST and the bone tissue was observed in the study group at day #14. Quantitative analysis with μCT (Fig. 2, B, C): There were no significant differences between two groups at day #28 in bone volume fraction, trabecular number, trabecular thickness, and trabecular separation.

**Discussion:** This is the first study to demonstrate the activated endothelial cells derived from muscle tissue can enhance healing of the tendon-to-bone as early as 2 weeks. According to previous literatures, tissue-specific endothelial cells establish specialized vascular niches that deploy sets of growth factors called angiocrine factors.<sup>6</sup> These factors may participate actively in the induction, specification, patterning, and guidance of tissue regeneration. Implanted mECs played a critical role in the healing and regeneration process of the SST from the early phase after surgery. mECs might be a promising cell source for the future treatment of soft tissue injuries.



**Figure 1** (A) Study design. (B) Cell tracking at day #3 and day #7. mECs were labeled with GFP. (C) Biomechanical tensile test. Failure force at day #14 and day #28.



**Figure 2** (A) Hematoxylin and eosin staining. Scale bar indicates 300 μm. (B) Representative Micro CT images at day #28. (C) Quantitative Micro CT analysis at day #28.

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**Paper #23 IS IT WORTH REPAIRING ROTATOR CUFF TEARS? A PROSPECTIVE COST-UTILITY ANALYSIS USING REAL WORLD DATA**

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**Introduction:** Knowledge about the costs and benefit of orthopedic surgeries in a real world setting is needed for orthopedic surgeons

**Table 1** Quality of Life (EQ-5D Index) and costs over time

	Year before surgery (SD)	First year after surgery (SD)	Second year after surgery (SD)	Incremental cost-effectiveness ratio (ICER)
<b>EQ-5D-Index [0-1] (n = 152)</b>	0.67 (0.24)	0.94 (0.11)	0.96 (0.06)	
<b>Direct medical costs in US\$ (n = 131)</b>	5,628	18,629	4,171	26,194/QALY
<b>Indirect costs in US\$ (work production losses) (n = 87)</b>	3,639	2,124	472	
<b>Total costs in US\$ (direct + indirect costs) (n = 131)</b>	8,045 (6,759)	19,975 (10,752)	4,443 (8,116)	18,296/QALY

**Table 2** Incremental cost-effectiveness ratio (ICER) of different patient groups (n = 113)

	ICER [US\$/QALY]	95% confidence interval
<b>Degenerative rupture (n = 46)</b>	31,988	12,579-51,398
<b>Traumatic rupture (n = 67)</b>	10,027	2,774-17,281
<b>Age&gt;60 (n = 48)</b>	27,777	6,595-48,959
<b>Age≤60 (n = 65)</b>	12,535	4,978-20,093
<b>Work pre-OP not reduced (n = 59)</b>	20,158	10,044-30,273
<b>Work pre-OP reduced (n = 23)</b>	3,903	3,784-11,589
<b>Age≤60 with traumatic rupture and/or pre-OP work reduction (n = 47)</b>	9,980	2,681-17,279

as well as social insurances and health policy decision makers. Little is known about the impact of arthroscopic rotator cuff repair (aRCR) on the quality of life and costs and whether particular patient groups benefit more from such interventions. We examined the influence of aRCR on the quality of life, direct medical costs and indirect costs (productivity losses) from the societal perspective.

**Methods:** Patients indicated for aRCR were included in a prospective study. Quality of life (EQ-5D-5L) and shoulder function were assessed one year before (pre-OP) and up to two years after surgery (post-OP). Health and accident insurance companies provided direct medical cost data for the same period including all health-related diagnoses to cover potential side effects of aRCR. Indirect costs were assessed using the work productivity and activity impairment (WPAI) questionnaire. Mean total costs to gain one extra quality adjusted life-year (QALY) were estimated by calculating the incremental cost-effectiveness ratio (ICER); 95% confidence interval (95%CI) was calculated using the non-parametric bootstrap method. The factors age, cause of rupture (trauma vs. degenerative), and degree of work reduction preoperatively were investigated as potential factors influencing the results using multivariate regression analyses and ICER calculation for patient subgroups.

**Results:** For 152 aRCR patients (mean age 56.8 years; 63% male), the mean EQ-5D index improved significantly after surgery and the mean total costs decreased below the pre-OP level in the second year after surgery (Table 1). Improvement in shoulder function was highly associated with improvement in the EQ-5D index ( $P < .001$ ). The ICER was 18,296 US\$ per QALY gained (95%CI: 9,646-26,946 US\$/QALY) until two years post-OP compared to the pre-OP control period. Patients with traumatic tears, who were up to 60 years old, or had to reduce their work preoperatively had lower ICERs (Table 2).

**Conclusions:** Arthroscopic RCR shows a cost-utility ratio clearly below the often suggested US\$ 100,000/QALY threshold in all patient groups. This ratio seems even more favorable in patients up to 60 years, patients with traumatic tears and patients who had to reduce their work preoperatively.

**Paper #24 NONOPERATIVE TREATMENT OF ATRAUMATIC, SYMPTOMATIC, FULL THICKNESS ROTATOR CUFF TEARS- FIVE YEAR FOLLOW-UP OF THE MOON SHOULDER GROUP COHORT**

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**Introduction:** 452 subjects were enrolled in a prospective multicenter study designed to assess predictors of failure of nonoperative treatment of symptomatic, atraumatic, full thickness rotator cuff tears. All patients underwent an evidence-based rehabilitation program.<sup>2</sup> At 2 years, 75% did not have surgery<sup>3</sup> and the strongest predictor of surgery was the patient's expectations regarding the outcome of treatment.<sup>1</sup> The purpose of this study was to assess the 5 year follow up and ascertain if patients were undergoing surgery as time progressed and review the predictors of surgery at 5 years.

**Methods:** 433 patients with atraumatic full-thickness rotator cuff tears who consented to enroll provided data via questionnaire on demographics, symptom characteristics, comorbidities, willingness to undergo surgery, and patient-related outcome assessments (Short Form 12 score, American Shoulder and Elbow Surgeons score, Western Ontario Rotator Cuff score, Single Assessment Numeric Evaluation score, and Shoulder Activity Scale). Physicians recorded physical examination and imaging data. Patients began a physical therapy program developed from a systematic review of the literature and returned for evaluation at 6 and 12 weeks. At those visits, patients could choose 1 of 3 courses: (1) cured (no formal follow-up scheduled), (2) improved (continue therapy with scheduled reassessment in 6 weeks), or (3) no better (surgery offered). Patients were contacted by telephone at 5 years to determine whether they had undergone surgery since their last visit.