using patient demographics and tumor characteristics. **Results.** Stage-specific survival was worse for young patients compared to older patients (Stage I, 86.1 vs. 91.8%; Stage II, 73.0 vs. 81.3%; Stage III, 58.3 vs. 66.8%; $P < 0.002$ for all stages). Younger patients present with more advanced disease than older patients (Stage I, 27.1 vs. 44.7%; Stage II, 48.1 vs. 36.3%; Stage III, 9.7 vs. 6.9%; $P < 0.001$ for all stages). Additionally, younger patients had more aggressive tumor characteristics per stage; that is, higher grade tumors and more estrogen and progesterone receptor negative tumors ($P < 0.001$ for both findings). A multivariate analysis showed that receptor status was the most important predictor of survival for patients with Stage II disease. **Conclusions.** Our findings show that younger breast cancer patients have poor outcomes because they present with later stage disease and stage per stage have more aggressive tumors. To address these issues, physicians need to have heightened awareness when evaluating breast abnormalities in this population, and increasingly efficacious adjuvant therapies need to be developed.

P12. **Does Higher Volume Predict Important Outcomes Other Than Mortality?** C. Y. Ko, M.D., M.S., MSHS, M. Maggard, M.D., and D. Zingmond, M.D., Ph.D. UCLA School of Medicine, Los Angeles, California.

Introduction. Most volume-outcome studies use mortality (usually inpatient) as the outcome variable; however, many surgical procedures have low death rates. The objective of this study was to determine the relationship between hospital volume and other clinically relevant discharge-related outcomes, for example, length of stay (LOS), and discharge facility type, like skilled nursing facility (SNF). **Methods.** Using the California State Hospital Discharge Database, all cases of colorectal cancer (CRC) resections from 1995 to 1999 were collected. Hospital volume was divided into four groups: <20, 21–40, 41–75, and >75 CRC resections per year. Statistical analyses were performed to identify the effect of volume on LOS (days), discharge facility (home, SNF, rehabilitation facility), and death. Comorbidity was adjusted for using a modified Charlson comorbidity index. Subsequent multivariate analyses were used to assess how good a predictor hospital volume is—compared to other clinically relevant variables. **Results.** A total of 56,704 CRC resections were included in the analyses. Using bivariate analyses, LOS, discharge facility type, and mortality differed statistically by hospital volume (see table). However, it should be noted that when analyzed with an adjusted model (i.e., multivariate regression analyses), comorbidities, surgical acuity, and age were all better predictors than hospital volume of LOS, discharge facility type, and death. **Conclusions.** While we found that higher volumes are statistically associated with improved discharge-related results, the relative importance of volume was small compared to comorbidities, surgical acuity, and age. While the implications of these results are controversial, high volume is still likely a proxy for good process of care.

P13. **The Prevalence of Sphincter-Sparing Procedures in Patients with Rectal Cancer: We Can Do Better.** C. Y. Ko, M.D., M.S., MSHS, J. Liu, M.D., D. Etzioni, M.D., and M. Maggard, M.D. UCLA School of Medicine, Los Angeles, California.

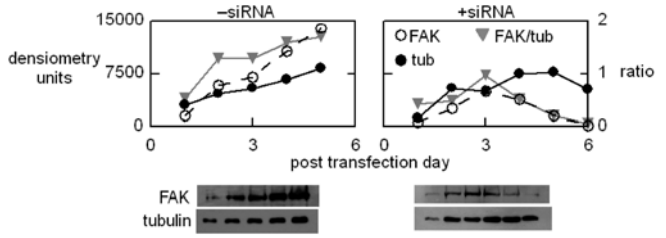
Introduction. Sphincter-sparing procedures (SSP) for rectal cancer are preferred because of the avoidance of a colostomy and better quality of life. In fact, the performance of an SSP is now being used an outcome measure and an indicator of surgical "quality." Since no population-based study has been performed regarding SSPs, we examined national rates of SSP versus abdominal–perineal resection (APR) over the past 15 years. Areas for improvement were identified. **Methods.** All patients with rectal cancer undergoing either SSP or APR from 1983 to 1998 were identified in the SEER database. Rates of both procedures were compared over three time periods (1985–1989 vs. 1990–1994 vs. 1995–1998), controlling for age, sex, race, and other variables. Predictors of SSP performance (or lack thereof) and survival were analyzed. **Results.** In 13,484 rectal cancer patients, average age was 67 years; 58% were male. Over the three time periods, SSP use increased (47% to 53% to 60%, $P < 0.001$). While females had more SSPs (57 vs. 49%, $P < 0.0001$), younger patients (<60 years) were less likely to have SSPs ($P = 0.01$). Racial disparities were also observed. For example, the use of SSP for stage 3 rectal cancer in Whites, Blacks, and Hispanics was 56, 44, and 45%, respectively ($P = 0.02$ vs. Whites). Noteworthy, stage-specific, 5-year survival was better for SSP versus APR ($P < 0.01$). **Conclusions.** In the United States, while the use of sphincter-sparing procedures for rectal cancer is increasing, areas of disparity are seen. Improved quality of life, and possibly improved survivals, may be achieved by further increasing the use of SSPs and by recognizing and addressing the areas where improvements may be made. This study has identified some of these areas.

P14. **RNA Interference of FAK in Primary Dermal Fibroblasts.** M. A. Carlson, M.D., R. E. Lewis, Ph.D., M. T. Longaker, M.D., and J. S. Thompson, M.D. University of Nebraska Medical Center, Omaha, Nebraska.

Introduction. Inhibition of gene expression with short interfering RNA (siRNA) duplexes, known as RNA interference (RNAi), has been described in established cell lines. We hypothesized that we could inhibit focal adhesion kinase (FAK) expression with RNAi in primary dermal fibroblasts. **Methods.** Subconfluent monolayer human fibroblasts (neonatal foreskin) were treated with transfection vehicle (OligofectAMINE; 0.5% in 300 μl; 24-well plate) or vehicle + 200 nM RNA duplex (AAUGGAGCGAGUAUUAAAGGU, corresponding to bp 328–348 of the human FAK gene) for 4 h. Relative FAK expression was calculated from densiometry of FAK and tubulin immunoblots. The experiment was performed twice with similar results. **Results.** Transfection of the FAK-specific RNA duplex resulted in virtually complete suppression of FAK expression

TABLE—ABSTRACT P12

Variable	<20	21–40	41–75	>75	*P* value
LOS-colon	9.8	9.7	9.1	8.8	<0.001
LOS-rectal	9.2	8.8	8.6	8.0	<0.001
D/C home (%)	62.6	66.7	70.0	72.1	<0.001
D/C SNF (%)	18.4	15.9	14.3	12.6	<0.001
D/C rehab (%)	1.05	0.98	0.71	0.41	<0.001
Hospital death (%)	4.70	3.55	2.70	2.41	<0.001
Comorbid index	0.93 ± 1.2	0.96 ± 1.3	0.91 ± 1.2	0.90 ± 1.2	=0.06



5–6 days after transfection (see figure). Tubulin expression was comparable between the control and siRNA-treated cells. Lysate (protein) of the treated cells was within 20% of the control value on any given day (data not shown). **Conclusions.** Treatment of human dermal fibroblasts in monolayer with siRNA specific for FAK resulted in specific knock-down of FAK expression. RNA interference is a novel technique which has great potential in the field of gene silencing; we have demonstrated its feasibility in primary human cells.

P15. **A Role for the Connective Tissue Enzyme, Semicarbazide-Sensitive Amine Oxidase (SSAO), in Wound Healing.** P. J. Boor, M.D., H. J. Hawkins, M.D., Ph.D., M. B. Trent, B.S., Y. Yang, M.D., and D. N. Herndon, M.D. University of Texas Medical Branch, Galveston, Texas.

Semicarbazide-sensitive amine oxidase (SSAO) is a connective tissue and serum enzyme that has been littlestudied. Serum SSAO levels are markedly depressed in patients with severe burns, and rising serum SSAO activity correlates with improved recovery. Our recent studies have shown that SSAO is essential for the development of elastin/collagen in connective tissues. Furthermore, aging-related decreases in SSAO activity may in part be responsible for defective ability to form mature connective tissue in aging patients. **Methods.** We examined SSAO alterations in human skin biopsies (1 week to 1 year) by immunohistochemistry, biochemical measurement of SSAO activity, and Western immunoblot analysis using highly specific antibodies to SSAO. Specimens included normally resolving cutaneous burns, hypertrophic scars, and keloids. **Results.** In normal skin or acutely following a burn (1 week) little or no SSAO staining was seen. However, at 3 weeks postburn, diffuse staining of both fibrovascular cells and interstitial tissues in the granulation tissue of healing burns became evident. At 3 months postburn, there was diffuse staining for SSAO in fibroelastic scar tissue. Keloids examined up to 1.5 years postburn showed the most prominent SSAO expression of any tissue by Western blot. The highly cellular, proliferative areas of keloids showed intense intracellular SSAO staining, suggesting that increased, persistent SSAO plays a role in formation of abnormal keloid connective tissues. **Conclusions.** These preliminary findings are consistent with our hypothesis that SSAO plays a major role in the formation and maturation of connective tissue components following burn injury of the skin. Most importantly, hyperexpression of SSAO is associated with the abnormal connective tissue formed in keloids. It is our hope that such studies may eventually lead to therapeutic manipulation of SSAO to improve outcome, enhance wound healing, and—potentially—prevent keloid formation in the burn patient.

P16. **L-Arginine Induces Wound Healing through Multiple Pathways in the Diabetic Wound Model.** R. P. Hanson, N. Sharifi, A. M. Byrne, D. C. Winter, and D. Bouchier-Hayes.

Introduction. It is well known that arginine, a unique substrate for inducible nitric oxide synthase (iNOS), improves wound healing in the normal and streptozotocin induced diabetic Sprague–Dawley rats. **Aim.** To investigate the effect of arginine on the expression of different proteins, cytokines, over time in the wound microenvironment over time, post-surgical insult. **Methods.** A total of 85 male Sprague–Dawley rats were used in this study. Sixty rats were rendered diabetic 7 days prior to surgery by a single intraperitoneal injection with streptozotocin (70 mg/kg). Twenty-five rats served as controls. All animals under went a 7-cm dorsal incision and insertion of polyvinyl-alcohol sponges. Thirty of the diabetic rats received 1 g/kg/day L-arginine in three divided doses by intraperitoneal injection. The remaining diabetic rats received an identical volume of normal saline also by intraperitoneal injection. Animals were euthanized on Days 1, 3, 5, 7, and 10. **Results.** We could demonstrate increased wound healing in the arginine supplemental group using hydroxyproline content as a parameter. The iNOS protein content in both diabetic groups was elevated at Day 1 compared to the control group ($P < 0.05$). The arginine-supplemented group maintained an elevated iNOS protein concentration that matched the control group throughout the experiment. The diabetic group failed to maintain this level and iNOS protein content decreased over time, reaching a significant difference at Day 7 compared to both the diabetic plus L-arginine group ($P < 0.05$) and the control group ($P < 0.05$). The level of transforming growth factor-β1 (TGF-β1) increases slowly over time in all groups. At Day 10, TGF-β1 in the diabetic plus arginine group is elevated toward the normal with significant difference compared to the diabetic group, ($P < 0.05$). **Conclusion.** The role of arginine in wound healing is multiple, while providing a substrate for the iNOS/arginase pathway it also induces transforming growth factor-β1 late in wound healing.

P17. **Effect of Vacuum-Assisted Closure Device on Rectus Muscle Pedicle Flap Venous Outflow.** A. M. Conquest, M.D., J. H. Garofalo, M.D., D. M. Maziarz, M.D., Y. Sun, M.D., K. Salleng, D.V.M., W. A. Wooden, M.D., FACS, W. M. Meadows, M.D., L. W. Nifong, M.D., and W. R. Chitwood, M.D., FACS. Department of Surgery, Brody School of Medicine, East Carolina University, Greenview, North Carolina.

Introduction. The vacuum-assisted closure device (VAC) has been shown to accelerate granulation tissue formation. We hypothesized that VAC-negative pressure adversely effects pedicle flap venous return and would preclude use of a VAC with a muscle flap. **Methods.** After institutional approval was obtained, 12 anesthetized pigs were divided into three groups. A rectus muscle pedicle flap was rotated over an open sternotomy wound. A laser flowmeter was placed on the superior epigastric vein and the VAC was applied to the wound. The pressures for Groups 1, 2, and 3 were 50 mm Hg constant, 125 mm Hg constant, and 125 mm Hg intermittent, respectively. Venous flow from the rectus muscle pedicle flap was monitored for 1 h during this acute study. Significance was determined by *t* test. The flap and control (contralateral rectus muscle) were harvested and histologic analysis was obtained. **Results.** The average venous outflow for the 12 animals was 13.8 ± 3.1 (ml/min/100 g tissue) (mean ± SD) prior to negative pressure application and 15.5 ± 5.4 (ml/min/100 g tissue) after 60 min of negative pressure ($P = 0.165$). No group experienced a decline in venous outflow during VAC function. On histologic examination, both flaps and controls showed comparable degrees of minimal to mild focal myocyte degeneration. **Conclusions.** Placement of a VAC over a rectus muscle pedicle flap does not significantly impair venous outflow from the flap and does not result in histologically significant ischemic injury or venous infarct to the flap.

P18. **Slit-3 Null Mouse Is a Model For Pulmonary Hypertension Secondary to CDH.** S. E. McLean, M.D., W. Yuan, Ph.D., R. Knutsen, B.S., D. M. Ornitz, M.D., Ph.D., and R. P. Mecham, Ph.D. Departments of Cell Biology, Molecular Biology, and Surgery, Washington University School of Medicine, St. Louis, Missouri.

Introduction. Pulmonary hypertension contributes to the morbidity and mortality associated with congenital diaphragmatic her-