intraoperative contraindications, the surgical procedure to which the patient was assigned was not done for about one in every seven surgeries—18% of patients assigned to DPPHR underwent a partial pancreatoduodenectomy and 13% of patients assigned to partial pancreatoduodenectomy underwent DPPHR.

Despite these limitations, these findings suggest that more than one surgical procedure could provide clinical benefit for patients with chronic pancreatitis. Still unknown is whether the varied approaches to partial pancreatoduodenectomy or DPPHR affect clinical response; how the risks and benefits of both interventions compare with other surgical procedures to treat chronic pancreatitis; the optimal timing for surgical intervention; whether the morphology of the pancreas affects surgical responses; and whether these findings from (on average) middle-aged adults with a history of smoking or drinking will translate to other populations of patients with chronic pancreatitis, including those with genetic mutations and severe disease in childhood. Head-to-head randomised trials of pancreatic surgery must continue to be done, although the diversity of the patient and disease population must be considered.

Thus, clinical trials are a crucial component of determining the right surgical approaches. However, as we enter the age of precision medicine, the question might not only be whether one surgical procedure is superior for all patients with chronic pancreatitis, but also whether we can select the surgery that is most likely to benefit a particular patient.

*Melena D Bellin, Gregory J Beilman
Department of Pediatrics (MDB) and Department of Surgery (MDB, GJB), University of Minnesota Medical Center, Minneapolis, MN 55454, USA
bell0130@umn.edu

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Penile transplantation is here

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Despite high initial mortality, the development of immunosuppressants has allowed solid organ transplantation to become a mainstay of modern medicine, providing a near cure for otherwise fatal conditions. Life-enhancing vascularised composite allotransplantation (VCA), such as face or hand transplantation, has increasingly been used to successfully treat devastating tissue loss. Results from a recent survey suggest that public attitudes in the USA are favourable overall towards the use of VCA, although concerns remain about seeing familiar body parts on the donor recipient, psychological discomfort, identity loss, and the need for lifelong immunosuppression to treat a non-life-threatening disease.[1]

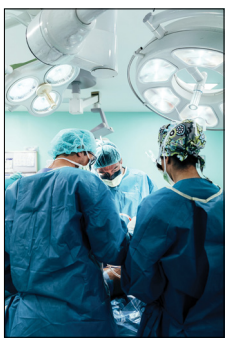
Given the personal and publicly unnoticeable circumstances of genitalia, penile disfigurement can be

seen as not being as socially debilitating as severe facial disfigurement or as incapacitating as loss of an arm or hand, and therefore might be subject to increased scrutiny of its value. However, human penile transplantation is an emerging technique to treat severe penile disfigurement. In *The Lancet*, André van der Merwe and colleagues describe the 24-month follow-up of a successful penile transplantation in a 21-year-old man in South Africa who lost his penis 3 years previously because of complications associated with ritual circumcision.[2] Ritual circumcision is a rite of passage, during which the foreskin is removed, often by use of a non-sterile instrument such as a spear, and the men are sent into seclusion for 1 week thereafter. Complications are common and include infections, which result in hundreds of hospital admissions every year and tens of penile amputations and deaths.[3] The young man in this Article lost his penis to a gangrenous infection and was treated with penile transplantation requiring lifelong immunosuppression. By the end of the 24-month follow-up, his graft remained viable, he was voiding spontaneously, he was having unaided natural erections, and he fully accepted his penile transplantation. However, these successes came with the price of surgical complications and episodes of rejection.

Van der Merwe and colleagues' report highlights the importance of genitalia to the human experience and personal perception of worth and reason to live, especially for a sexually active young man. Arguments are made that reconstructive options, including neophallus surgery, can address severe penile disfigurement. The two most common neophallus construction methods use tubularised soft tissue from the forearm or the anterior lateral thigh, which is transferred to the location of the penis.[4] However, constructing a neophallus might not be possible in men who have inadequate tissue donor sites, such as soldiers who have suffered limb injury. Additionally, neophalluses suffer from complication rates approaching 40% in some series.[5] These complications include urinary fistulas and urethral strictures that can require several additional operations to correct.[5] Penile transplantation is not devoid of these complications either.[2] The penile transplant recipient discussed in the report developed a urinary fistula at the anastomosis site associated with voiding through the urethra on postoperative day 8 when the suprapubic tube was obstructed by a blood clot, which was successfully surgically corrected 3 months after the operation.

Neophalluses also have no inherent erectile function.[5–7] Understanding of the neophallus comes mostly from its use in transgender operations and for treating congenital defects.[5–7] Reports suggest that individuals treated with a neophallus are considerably less likely to engage in penetrative intercourse than a sexually active young man.[8] Van der Merwe and colleagues underscore the high extrusion rate of neophallus penile prostheses, poor access to specialised reconstructive techniques, and the costs associated with penile prosthesis and neophallus complications in South Africa, where there is a substantial population of men with severe penile tissue loss secondary to complications of ritual circumcision.[2] By contrast with a patient having to wait an average of 1 year for a penile prosthesis to be implanted into a neophallus, the penile transplant recipient in this study experienced spontaneous natural erections 3 weeks after surgery and, despite medical advice to the contrary, had successful sexual intercourse at 5 weeks and was later able to impregnate his partner and have sexual intercourse without erectile aids by 6 months post transplant. Most importantly, the patient expressed early acceptance and sustained satisfaction with his transplanted penis, as shown by the near doubling of his mental health score to normal levels after receiving the transplant. He described the most important result of his transplant being that he is "happy" again, which he attributed to the restoration of all components of penile function. Both reconstructive options and penile transplant require substantial medical resources and expertise that might not be available in resource-poor locations. However, the needs of men in resource-poor settings might not be met with reconstructive options, as these require repeat procedures with expensive, complication-prone implants to make them sexually active and involve deformation of donor sites (such as the arm) that could prevent manual work. Van der Merwe and colleagues' report suggests that, after the initial acute postoperative period, a transplanted penis might be fully functional and not require additional procedures, but does require frequent immunosuppression monitoring and adjustment, which are not trivial in remote locations.

Despite these promising results, much work is needed. Although this report suggests the surgical feasibility of penile transplantation, its biology is poorly understood. As seen in solid organ transplantation and other forms of VCA, different tissues reject differently, and thus



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immunosuppression regimens vary depending on the organ. The penis is a complex organ composed of many different tissue types including skin, connective tissue, vascular sinuses, extensive innervation, and urothelium. It is unclear how these tissues will reject, how rejection will affect its function, how to best monitor the penis for rejection, and which immunosuppression regimen is optimal. Indeed, reports suggest that ciclosporine A might impair erectile function, stressing the importance of preclinical research in this developing area of VCA.[5,9,10] Additionally, immune tolerance is an active area of research[11] that seeks to reprogramme the recipient's immune system to accept donated tissues, with the goal of reducing the amount of, or need for, traditional immunosuppression. Additional research regarding the ethics and clinical application of penile transplantation, including the adoption of guidelines, is needed to ensure safe and ethical use. These potential improvements will help to lower the risks and increase the application of transplantation to address difficult-to-treat conditions.

*Nikolai A Sopko, *Arthur L Burnett*
The James Buchanan Brady Urological Institute and Department of Urology, The Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA
aburnet1@jhmi.edu

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Early-stage breast cancer: falling risks and emerging options

Dr P Marazzi/Science Photo Library

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Great improvements in the therapeutic ratio of cancer treatment can result from innovative approaches that maintain tumour control benefits while lowering treatment-associated morbidity. The IMPORT LOW trial by Charlotte Coles and colleagues[1] in *The Lancet* is a high-quality randomised trial of treatment de-escalation in the multidisciplinary management of breast cancer.

Numerous trials and their meta-analyses have established that after breast-conserving surgery, radiotherapy cuts the risk of recurrence by half and reduces breast cancer mortality.[2] However, this treatment can also result in serious morbidity due to the incidental irradiation of normal tissues, including the heart, lung, and normal breast.[3,4]

Partial-breast irradiation reduces the dose to normal tissues by treating only the region surrounding the tumour bed (the site of most local failures) rather than the traditional radiotherapeutic target (the whole breast). By reducing the volume of tissue irradiated, particularly when using advanced techniques that allow highly conformal dose distributions, the number of treatments needed could be reduced by allowing higher doses per treatment fraction than conventionally administered to the whole breast. Indeed, many trials have investigated or are investigating the simultaneous reduction in the treatment field and increased radiation dose per fraction in an attempt to reduce not only toxicity but also the burden from multiple repeated treatments.[5–7] By contrast, IMPORT LOW used a relatively simple technique to reduce the volume of treatment, while holding radiation dose and fractionation constant.

The control group received a whole-breast regimen of 40 Gy radiotherapy daily in 15 fractions. The experimental groups had treatment in the vicinity of the tumour bed