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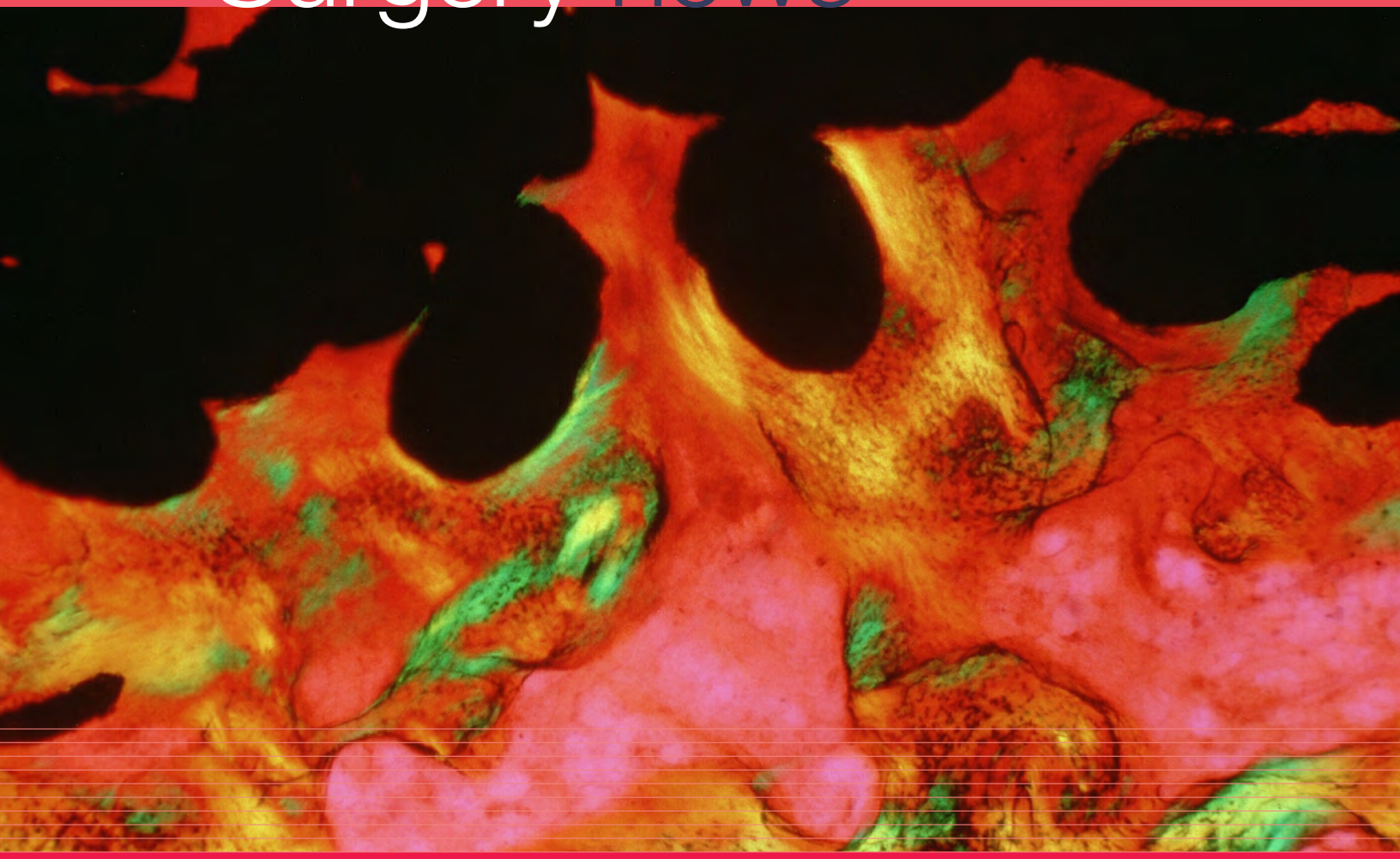

Percutaneous Osseointegration Offers Amputees New and Better Options

When Swedish researcher Per-Ingvar Brånemark completed the first human dental implant in 1965, the procedure demonstrated the advantages of creating a functional and structural connection between living bone and an artificial titanium implant. He called the concept "osseointegration," and 25 years later, Swedish surgeons completed the first bone-anchored percutaneous osseointegrated implant for an above-the-knee amputee.

Now, after 2015 FDA approval, Brånemark's son – Rickard Brånemark, MD, PhD – is bringing these implants to the US as a visiting professor in the UCSF Department of Orthopaedic Surgery. A UCSF Presidential Chair, Brånemark also leads the newly created international Center for Osseointegration Research, Education and Surgery (iCORES). His co-director is Richard J. O'Donnell, MD, a pioneer in compressive osseointegration,

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Message from the Chair

Thomas Parker Vail, MD

Our goal in the Department of Orthopaedic Surgery is to continually improve our patients' musculoskeletal health, in part by rigorously exploring new approaches to meeting the most pressing challenges.

With that said, the department is thrilled to have Rickard Brånemark, MD, PhD, join our faculty. He brings truly pioneering experience with percutaneous osseointegrated implants, which are stronger, more natural artificial limb solutions for many military and civilian amputees. The implants attach directly to the skeleton and avert common problems with socket fitting and pain.

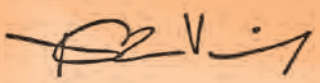
Similarly, surgeon Stefano Bini, MD, is studying and offering patients personalized approaches to knee replacement that focus on understanding the original prearthritic joint line and the relationship to the knee's natural rotational axis. The goal is to create a more natural-feeling knee, which becomes a silent part of the patient's anatomy.

Andrew Brack, PhD, a muscle stem cell scientist, is working with orthopaedic and plastic surgeons to dramatically accelerate progress toward human muscle tissue regeneration. The goal of his work is to help patients whose muscles have lost their regenerative capacity, such as those with severe muscle injury, paralysis or childhood dystrophies.

Another clinical innovator, Conor O'Neill, MD – the new director of our nonoperative spine program – recently joined the Spine Center and brings decades of experience exploring minimally invasive ways to treat patients with complex back and neck pain.

Finally, foot and ankle specialist Daniel Thuillier, MD, expands our program to the Marin clinic, including access to total ankle replacement as an alternative to bracing and fusing bones for patients with end-stage ankle arthritis.

In the end, we are expanding our specialized clinical care in an effort to work with you to deliver evidence-based innovations that give our shared patients every opportunity to lead full and healthy lives. ▣



Thomas Parker Vail, MD
James L. Young Professor and Chairman
Department of Orthopaedic Surgery

Percutaneous Osseointegration Offers Amputees New and Better Options

CONTINUED FROM FRONT COVER

which UCSF helped develop and which has long been used for limb salvage in cancer patients.

Along with Rosanna L. Wustrack, MD, iCORES has secured institutional review board (IRB) approval to complete the percutaneous procedures for amputees at UCSF Medical Center. A pending Department of Defense (DOD) grant with Walter Reed National Military Medical Center would provide funding to roll out the implants in a controlled, multicenter study for both above-knee and above-elbow amputees.

"While not appropriate for patients with peripheral vascular amputations, these implants provide exciting options for active-duty military and veterans with combat-related injuries, civilians with traumatic injuries, and tumor patients, all of whom bear an enormous burden," says O'Donnell.

Proven Success Around the World

In addition to continually refining the titanium implants and instrumentation – and performing the procedure in more than 200 Swedish patients – Rickard Brånemark has played a central role in bringing this approach to 12 other countries around the world.

"Globally, about 400 patients have the implants in trans-humeral, transradial and transtibial settings – and we've demonstrated a 90 percent success rate in Europe," says Brånemark.

In the procedure:

- Surgeons insert a titanium screw through the skin and into the femoral or humeral canal.
- The device remains in place for six months to allow bone to grow around it so that it can serve as a firm anchor for the prosthetic limb.
- In the ensuing months, patients increase weight bearing with their new prosthetic device.

"The implants are stronger and more natural for transferring loads to the prosthetic component and avoid common socket problems, such as tenderness, chafing and mobility restrictions," says Brånemark. Risks include bone or soft-tissue infections and occasional fracturing.

Rickard Brånemark, MD, PhD

Richard J. O'Donnell, MD

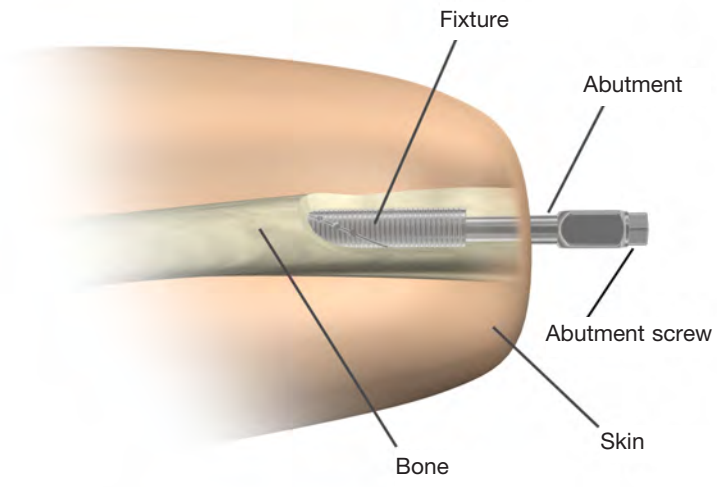
iCORES Delivers Team-Based Care and Innovation

The iCORES clinic is a collaborative effort involving not only surgeons, but also expert nurses, physical therapists, prosthetists and researchers who will help to translate next-generation projects for human use.

The most immediate project – which has generated considerable interest from within the DOD and elsewhere – involves bidirectional communication between the central nervous system and external upper extremity implants. In *Science Translational Medicine,* Brånemark recently profiled his first patient using such a device.

"We have wireless systems today, but our system can pick up the signal directly from the source with much higher accuracy and precision," says Brånemark. "We expect to make UCSF the leading center in the US for this kind of robotic technology." ▣

For more information, contact iCORES at 415-885-3800 or icoresinfo@ucsf.edu.



OPRA: Osseointegrated Prostheses for the Rehabilitation of Amputees

Personalized Total Knee Replacement and Alignment

A 75-year-old man with bilateral osteoarthritis underwent what appeared to be a successful total right knee replacement, but after a long and painful recovery, he refused to go ahead with a left knee replacement. His surgeons struggled to understand what went wrong.

It turns out these types of struggles are not uncommon. Despite long-held assumptions that standard knee replacements were working well, recent studies in the US, Canada and the UK have found that as many as one in five patients complain of pain, stiffness and/or instability – and are not completely satisfied with the replacement. Advances in computer-aided alignment have not solved these concerns.

"Consequently, some began to wonder if precise mechanical alignment was the problem, since it demands that the knee's joint line be perpendicular to the tibial axis and centered on a line that bisects the hip, knee and ankle," says UCSF orthopaedic surgeon Stefano Bini, MD. "Because very few people have such perfect alignment, a mechanically aligned knee is often forced to rotate around what is essentially a nonanatomic axis."

The concern led to a new way of thinking about total knee replacements and a new perspective on knee alignment. Bini believes that anatomic alignment can restore the prearthritic joint line and the knee's rotational axis, thus enhancing functionality.

Dr. Bini explains customized implants.

Improving Function, Satisfaction

"Essentially, we customize the implant's position to each patient's unique anatomy," says Bini. The 75-year-old man referred to above ultimately underwent an anatomic revision procedure for his left knee and was much happier with the results.

Studies have begun to determine the relationship between alignment and greater levels of satisfaction with a focus on:

- Improved flexion
- Improved extension
- Less stiffness
- Less pain

As the studies proceed, Bini notes that the instrumentation is evolving to make the restoration of alignment and the bending axis of the knee more reproducible. Major orthopaedic equipment manufacturers clearly recognize the potential of this avenue of clinical investigation.

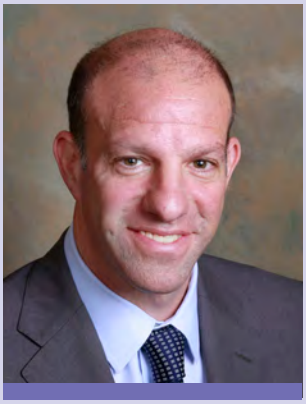
Bini is also conducting clinical research to confirm that replicating each individual's natural alignment can achieve improved results, and to better understand the biomechanics of anatomic alignment.

"Anatomic alignment doesn't solve all knee replacement problems, but it appears to solve many," says Bini. "It's an evolutionary approach and it's up to us to refine it." ▣

For more information, contact Dr. Bini at 415-353-2808.

Muscle Regeneration on the Verge of Clinical Application

Andrew Brack, PhD



Jason Pomerantz, MD

Collaboration between UCSF Department of Orthopaedic Surgery researcher Andrew Brack, PhD, and UCSF plastic and reconstructive surgeon Jason Pomerantz, MD, is accelerating progress toward treatments for patients with severe muscle injury, paralysis and other conditions – including aging – in which muscles lose their regenerative capacity.

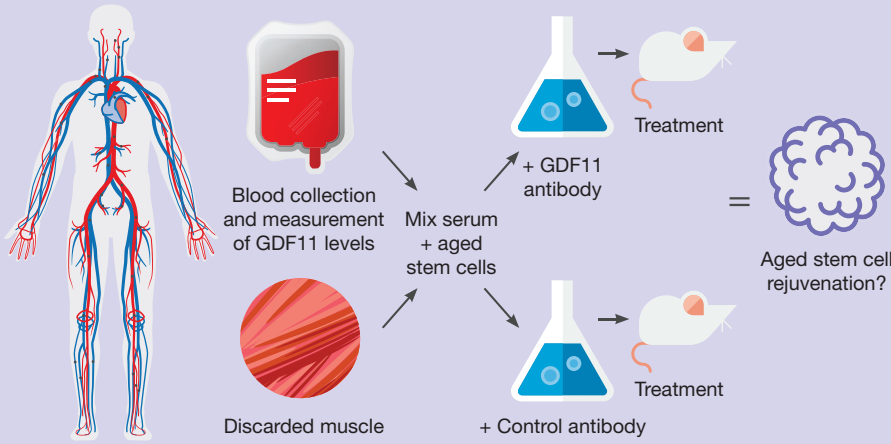
Brack studies the mechanisms of muscle aging. His work has been instrumental in establishing that the protein GDF11 is elevated in the blood of the elderly and that it blocks skeletal muscle regeneration.

Pomerantz recently led a team that successfully isolated human muscle stem cells and showed that these cells could replicate and generate human muscles when injected into an injured mouse muscle.

Now the two researchers will test whether introducing human muscle stem cells in combination with patient-matched blood of different ages and inhibiting production of GDF11 – which they will inject into mouse hosts – can replicate and amplify the results of their individual work.

"Our work builds on 20 years of muscle stem cell work in mice and allows us to discuss clinical applications in the very short term," says Brack.

Testing advances in muscle regeneration



"We're hopeful that within two years, this work will lead to a clinical trial that tests whether we can boost stem cell function and accelerate the muscle repair process for surgical patients," says Pomerantz.

A Great Leap Forward

Though surgeons have shown they can restore nerves in damaged muscles, until now the failure of the stem cell pool to repopulate quickly enough has undermined the muscles' ability to connect with the nerves and recover.

"This is partly why we haven't had major progress in treating these patients in 30 years," Pomerantz says. "We know we can get the axons there, but we need the stem cells for there to be recovery."

Pomerantz's work has shown that grafting human tissue into mouse hosts and introducing the muscle stem cells accelerates the process in a way that enables damaged tissue to heal. Inhibiting GDF11 activity could further accelerate the process.

Thus, Brack expects that the study he and Pomerantz are conducting will quickly lead to improvements in treatments for congenital muscle disease like muscular dystrophy, as well as for sports, spinal and combat injuries. Down the road, slowing the aging process and accelerating repair in skeletal muscle could enable more active lifestyles much later in life.

Both researchers say this approach is safer and more efficient than existing approaches, like human growth hormone, because it targets the specific areas in need of repair, rather than working systemically.

"In the last year, studying the muscle regeneration process in humans is now possible," says Brack. "If our study works as expected, it's a strong argument for a clinical trial." ▣

For more information, contact Dr. Brack or Dr. Pomerantz at 415-502-0515.

A Comprehensive Approach for Treating Complex Back and Neck Pain

After several months of low back and radiating left leg pain so severe he couldn't engage in physical therapy, a 45-year-old man had an MRI scan, which showed L4-5 disc bulging. He was concerned he needed surgery, but a comprehensive clinical evaluation found his type of back and leg pain was not typical for disc pathology.

Further review of his MRI showed facet degeneration at L5-S1, where he was tender on examination. A corticosteroid injection allowed him to engage in physical therapy, and six weeks later he was pain free. Follow-up education helped him understand that disc bulging – nearly universal with aging – rarely causes serious symptoms, particularly if he maintained a daily exercise regimen.

One year later, he had only minor, sporadic back pain.

Rooting Out the Pathology of Pain

"We have to be careful about making assumptions about the relationship between imaging studies and pain," says Conor O'Neill, MD, the newly appointed director of the UCSF Department of Orthopaedic Surgery's nonoperative spine program.

"Many times patients will complain of pain that doesn't correlate well with findings on the MRI scan – and appropriate treatment means sorting out this relationship between the structural pathology and the patient's symptoms," says O'Neill, who brings decades of experience working with back and neck pain to UCSF.

While expert surgeons can dramatically improve the lives of patients with clear-cut structural problems, O'Neill says the source of approximately 90 percent of patients' back and neck pain is less defined. Studies have shown these patients typically do just as well without undergoing the risks of surgery.

"Pain is a complex phenomenon that certainly includes structural problems, but many other factors as well, including psychological and social factors," says O'Neill. "Because we can't treat what we can't diagnose, we focus first on expert diagnosis that combines a careful clinical evaluation, spine imaging and, when needed, precision diagnostic injections."

Dr. O'Neill with a patient

A Full Menu of Nonoperative Treatments

Once physicians make their diagnosis, they choose from a range of treatment options, using their experience to match the right treatments with the right diagnosis. Those treatments might include:

- Physical therapy
- Exercise
- Chiropractic
- Acupuncture
- Medications
- Spine injections

"The other key element is patient education – helping patients adjust their outlook and lifestyle," says O'Neill, noting that most back and neck pain is degenerative and, therefore, will present in different ways at different times throughout a person's life. If patients understand that, they are better prepared for those changes and more likely to follow through with appropriate maintenance.

"It's important that we help patients recognize the difference between what their back looks like on an MRI and their pain, de-escalate their tendency to magnify the importance of findings and emphasize the need to keep their back and whole body in shape to prevent future episodes," says O'Neill, who is focused on tracking outcomes and costs to ensure his team continues to deliver high-quality, value-based care. ▣

For more information, contact Dr. O'Neill at 415-407-0342.

Bringing Partnership and Subspecialty Care to Marin

With the opening of a weekly Monday clinic right next to Marin General Hospital, at 1100 South Eliseo Drive in Greenbrae, the UCSF Department of Orthopaedic Surgery's foot and ankle service has extended access to its experienced specialists, who evaluate and manage all disorders of the lower leg, ankle and foot. These include complex foot deformities that require reconstructions or joint replacement.

"The clinic offers consistency and convenience for all patients, but especially for those experiencing more complex problems," says Daniel Thuillier, MD, who directs the clinic.

The Example of Total Ankle Replacement

One example of a complex problem that in the past would have required patients to make multiple trips into San Francisco is total ankle replacement (and, sometimes, revision ankle replacement), a procedure for which Thuillier has a particular expertise.

"Historically, the only good option for ankle arthritis was fusion," he says. "But today we can often get better results with ankle replacements, especially in older patients." He notes that newer replacement procedures can be done in stages and are tailored to each patient's unique anatomy.

Though such procedures are not without expected risks, such as wound healing problems and misalignment, when completed correctly, the newer ankle replacements are showing 90 percent satisfaction rates and improved longevity; they often last more than 10 years.

"Any patient experiencing ankle arthritis is a potential candidate," he says. "And now we can do the physical examination and X-ray and discuss the pluses and minuses of replacement versus fusion with patients right here in Marin. Ultimately, of course, the decision is theirs."

If they choose total ankle replacement, Thuillier will do the procedure at UCSF Medical Center in San Francisco. "But we work closely with referring physicians to help patients through recovery – and they can return to our Marin clinic for follow-up visits so we can monitor healing," he says.

Dr. Thuillier at work in the Marin clinic

A Full-Service Clinic

He adds that the clinic is also available for patients with less complex problems and is staffed and equipped for standard diagnostic procedures and routine treatments, such as casting and splinting.

"We have always had a lot of patients come to us from Marin, and we established this clinic so these patients can avoid unnecessary trips into San Francisco," says Thuillier. ▣

For more information, contact Dr. Thuillier at 415-353-2808.

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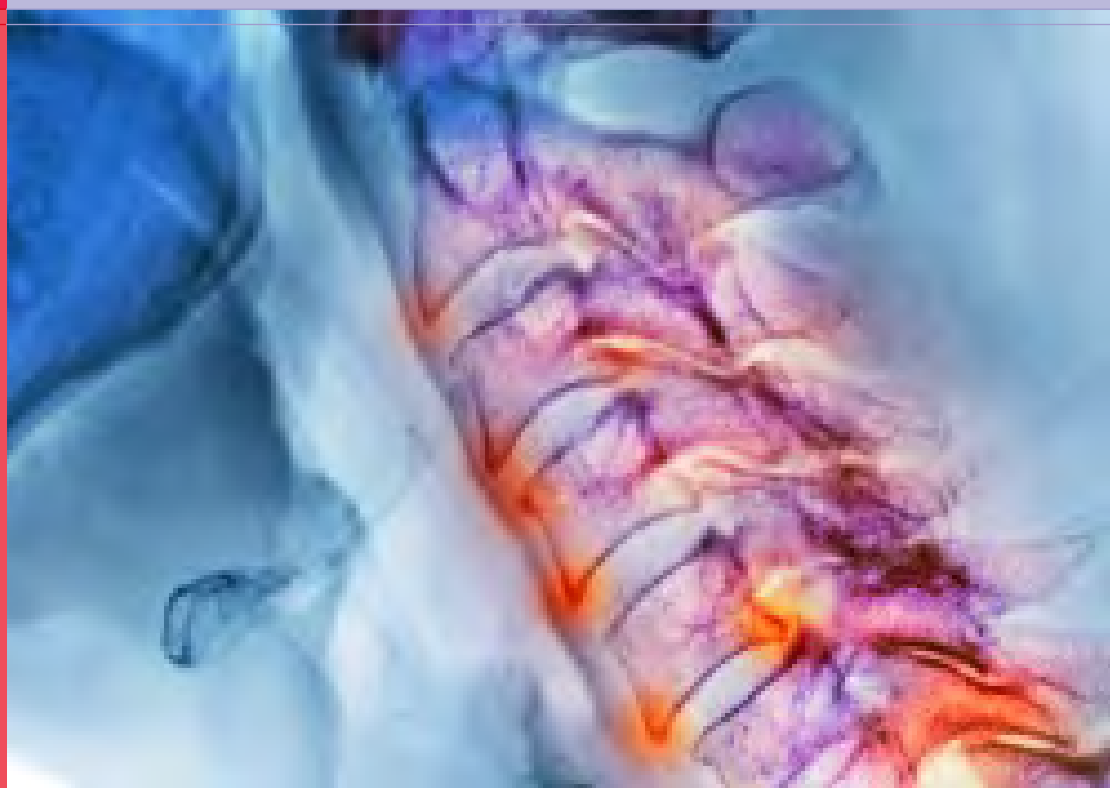
CME Courses

For more information, visit www.cme.ucsf.edu

11th Annual UCSF Spine Symposium	June 3-4, 2016	San Francisco, Calif.
6th Annual UCSF Techniques in Complex Spine Surgery Program	Nov. 4-5, 2016	Las Vegas, Nev.



Mark R. Laret, Chief Executive Officer, UCSF Health

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