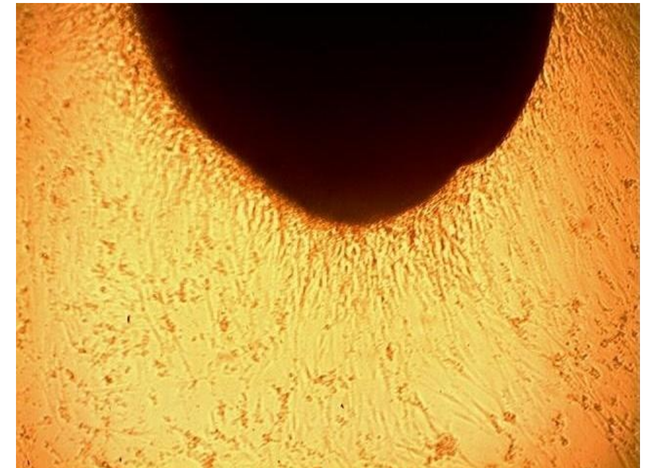
Regenexx Procedure: Imaging Case Reports and Medical Provider Information

www.regenexx.com

Regenerative Sciences

The Regenexx procedure is a patent pending autologous mesenchymal stem cell (MSC) transplant. This is a true “needle out/needle in” procedure that allows the physician to harvest MSC’s via fluoroscopic guidance, isolate a pure MSC population, culture expand those MSC’s to much larger numbers, and then deploy those MSC’s using MRI planned fluoroscopic guidance. The implant procedure varies with regard to cell preconditioning in culture, scaffold, and interventional technique based on the target tissue being repaired. For example, disc repair strategies are very different than tendon which are again different from fracture non-union. In addition, while percutaneous procedures are highlighted here, cells can be expanded for use with existing surgical procedures. These slides contain a sampling of imaging case results. For more information, contact centenooffice@centenoclinic.com.



Multiple types of tissue regeneration are highlighted. This is because MSC’s can differentiate into cartilage, bone, muscle, and tendon.

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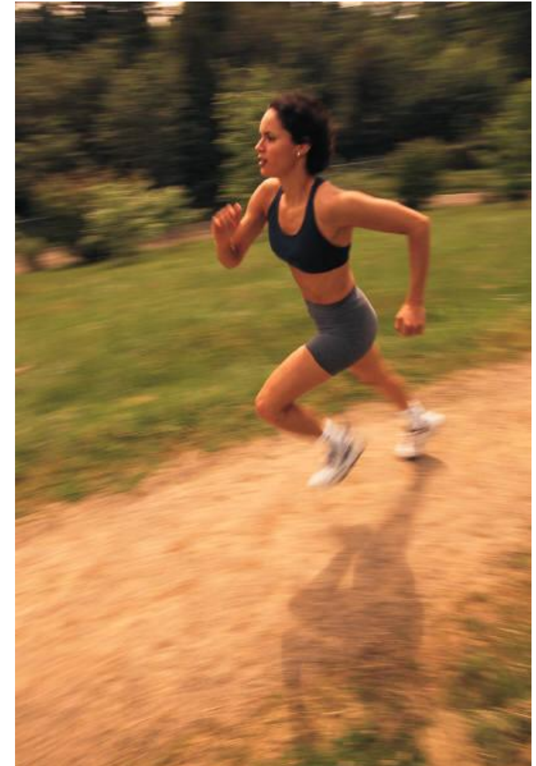


Activity Levels and the Regenexx Procedure

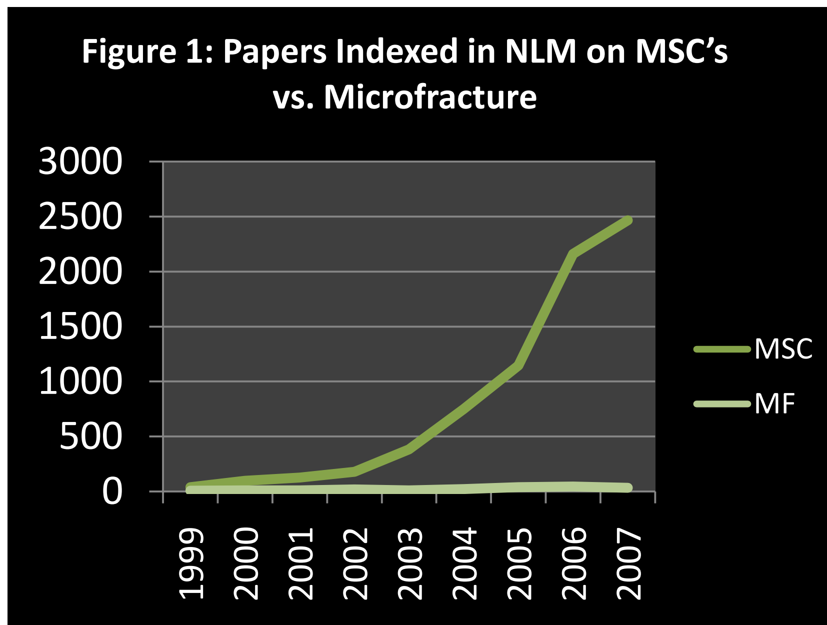
Unlike many surgical procedures that require extensive downtime, the Regenexx procedure only requires slight limitations of activity. For example, while a surgical micro fracture procedure or tendon repair might require being immobile for many weeks, Regenexx actually works better with limited activity (such as walking) immediately after the procedure. Why? Mesenchymal stem cells get clues from their environment about how to differentiate. For example, stretching or pulling forces causes them to become tendon cells. Compressive loading like walking, pushes these cells to become cartilage cells. As a result, we want you moving and being active as early as possible.

SUMMARY OF REGERATIVE SCIENCES RESEARCH

The Regenexx procedure was ported from a large animal model with the help of John Kisiday, Ph.D. (formerly of the MIT Mecahnobiology Dept). Major development on the clinical procedure and continued biotech development continued under the supervision of Christopher J. Centeno, M.D. 2005-2006 focused on changes to the procedure to allow autologous isolation and culture expansion of human mesenchymal stem cells without exposure to non-FDA approved substances (minimal manipulation). 2006-2007 focused on pre and post 3.0 T MRI follow-ups of cartilage, bone, and fibrous tissue regeneration targets. Since 2005 a long-term tracking database has been maintained following pain/functional status, blood work, 3.0 T MRI, and other parameters. No significant complications have been reported. Late 2007 was the start of commercial knee patients. Additional commercial applications were added as MRI data became available. Generalizability data is not yet available for each procedure, but case series data has been submitted for publication. Clicking on this link will bring you to an updated author search at the National Library of Medicine for Dr. Centeno.

SUMMARY OF BASIC RESEARCH ON MESENCHYMAL STEM CELLS UP TO 2008

Mesenchymal stem cells (MSC's) are adult progenitor cells which live in many tissues. They are general purpose repair cells for bone, cartilage, muscle, fibrous tissue, and other tissues. As figure 1 shows, when compared to surgical research topics (in this example micro fracture surgery (as a control)) MSC research has exploded.



Most of the MSC research published to date has been in animal models. Robust evidence exists (hundreds of studies) regarding the ability of MSC's to regenerate cartilage, bone, and muscle. Early human studies are just beginning to be published, with promising nascent results . To date, about 5,000 studies are indexed in the national library of medicine. To see this search result, click here.

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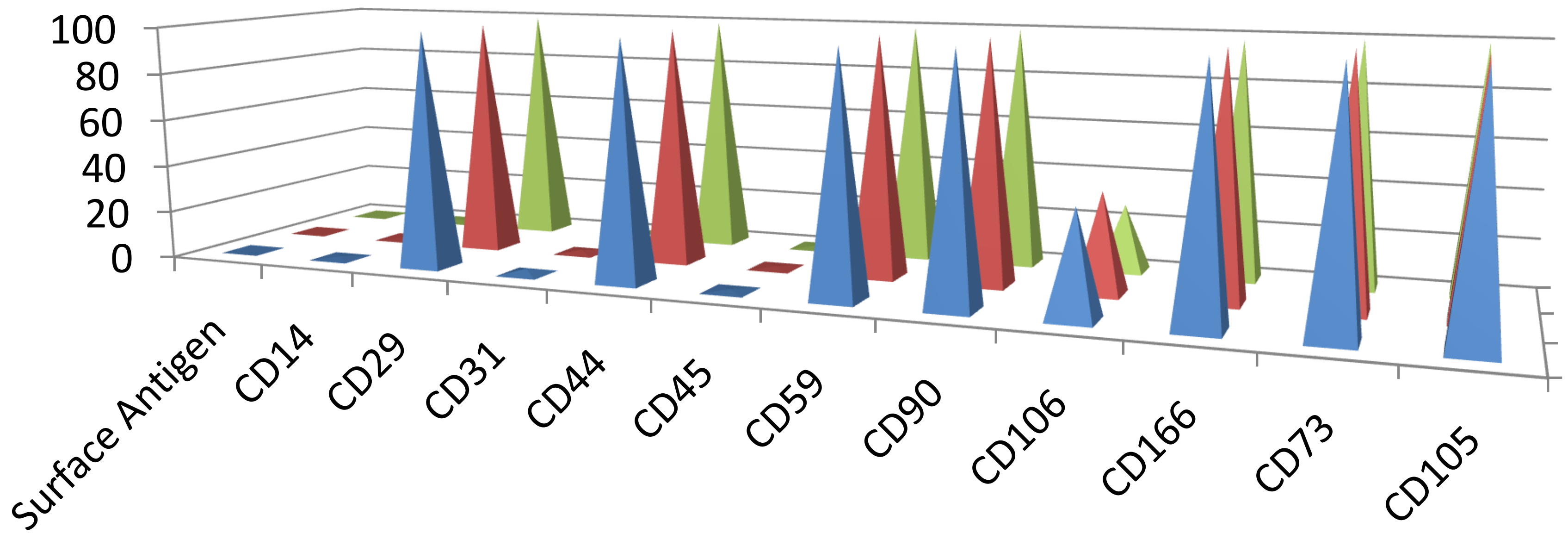
Surface Antigen Expression using FACS for Three MSC Lines Grown with Regenexx Procedure



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CASE REPORTS

All case reports are with pre-post 3.0T MRI performed on the same scanner with identical imaging sequences and the same or nearly identical imaging parameters.

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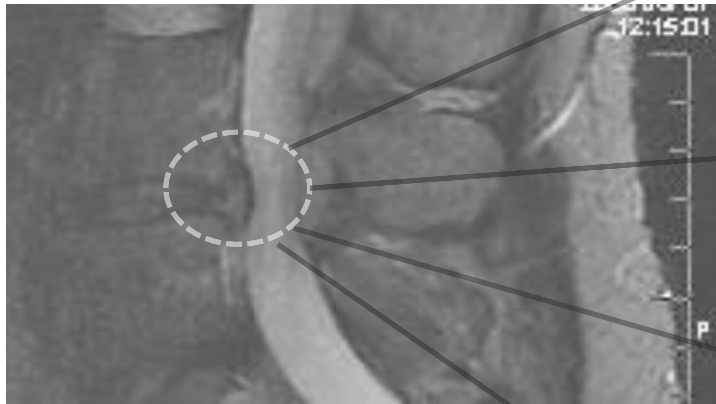
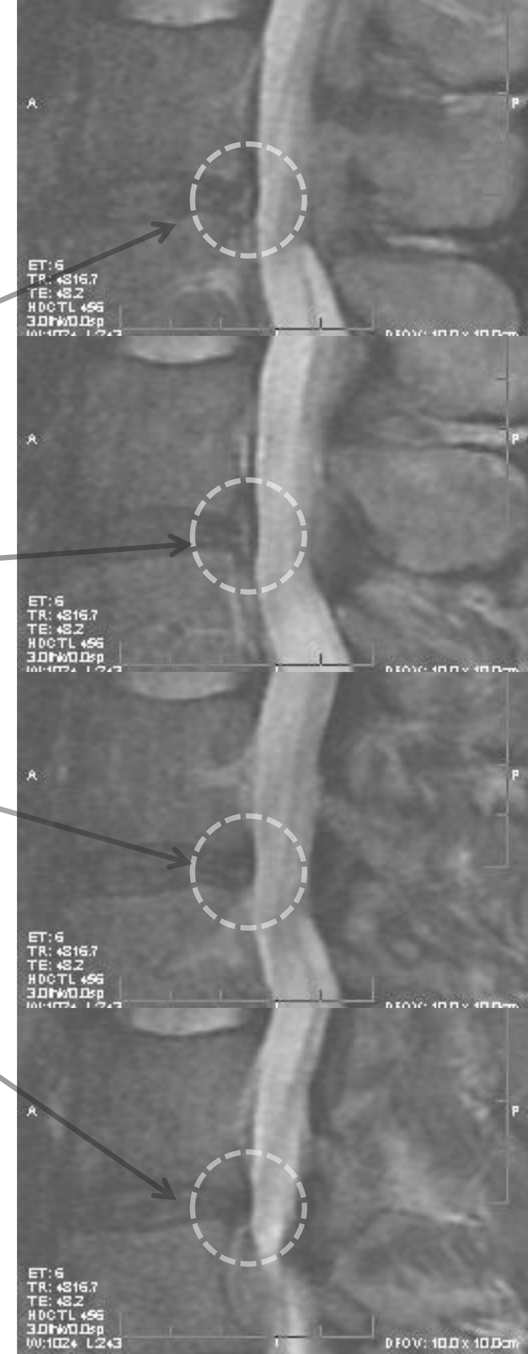
35 year old WM with chronic L4-L5 disc bulge and positive discography. Dramatic improvement in symptoms.



Before



2 Mo After: Slices Across Disc

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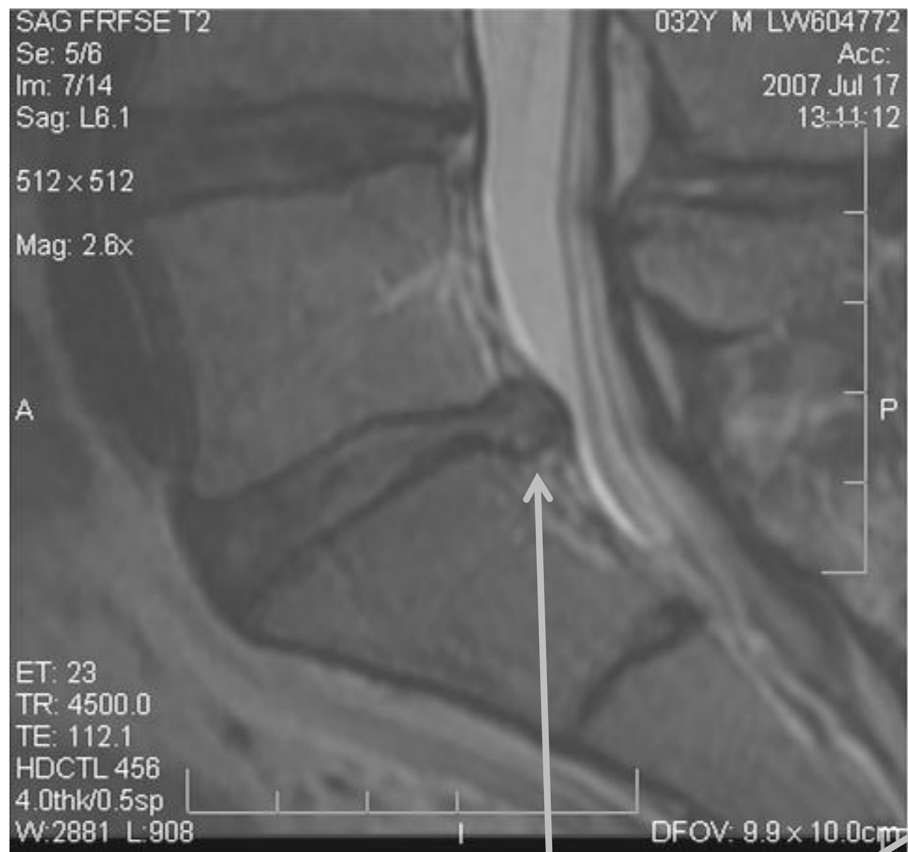

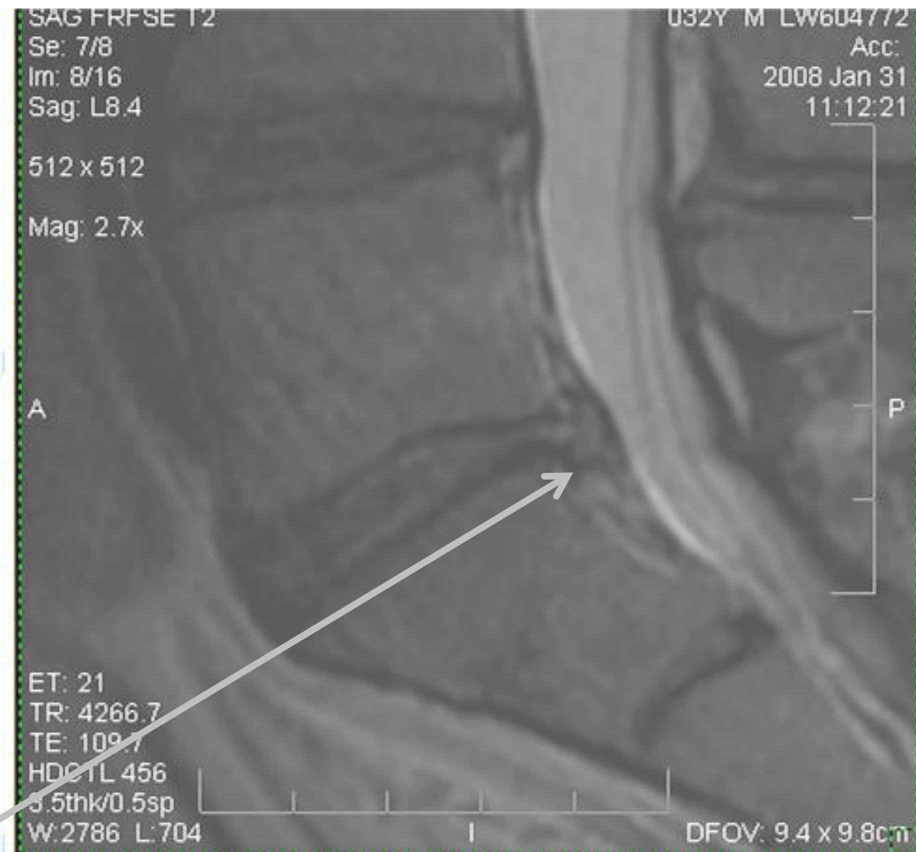

32 yo WM with many year history of chronic lumbar radiculopathy due to central L5-S1 disc bulge causing compression of bilateral; S1 nerve roots. Elimination of leg pain at 3 months after procedure. 3 month f/u MRI on right shows significant reduction is size of disc bulge.

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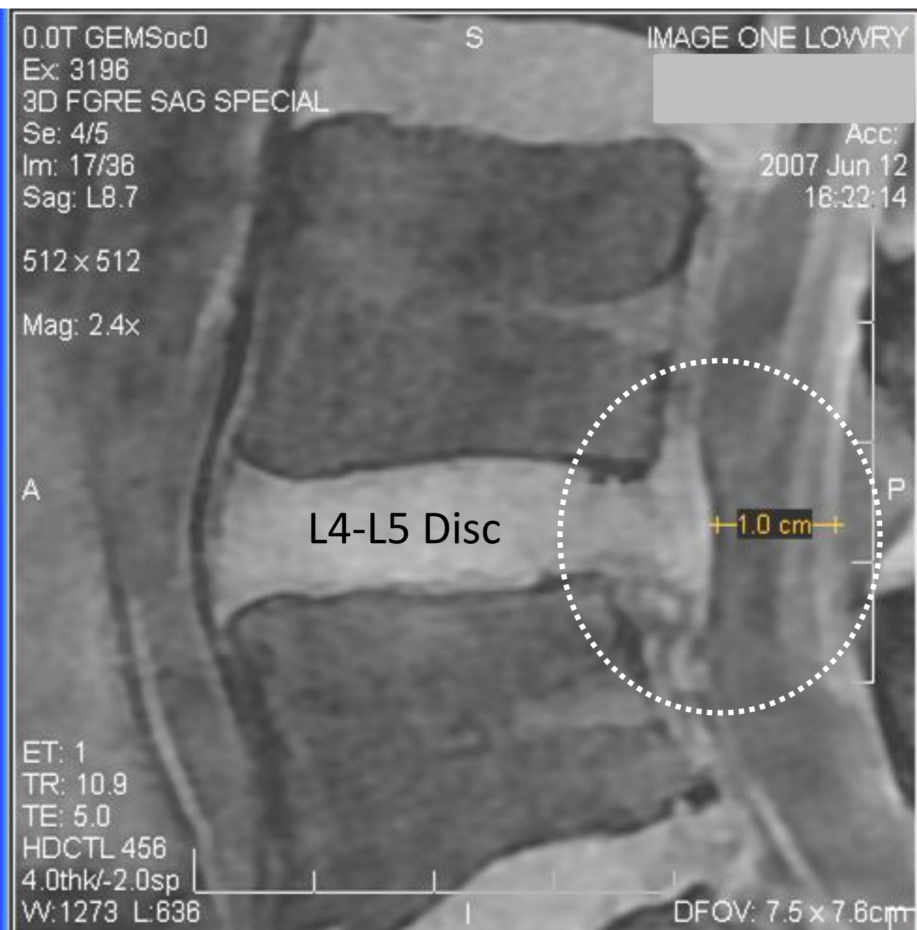

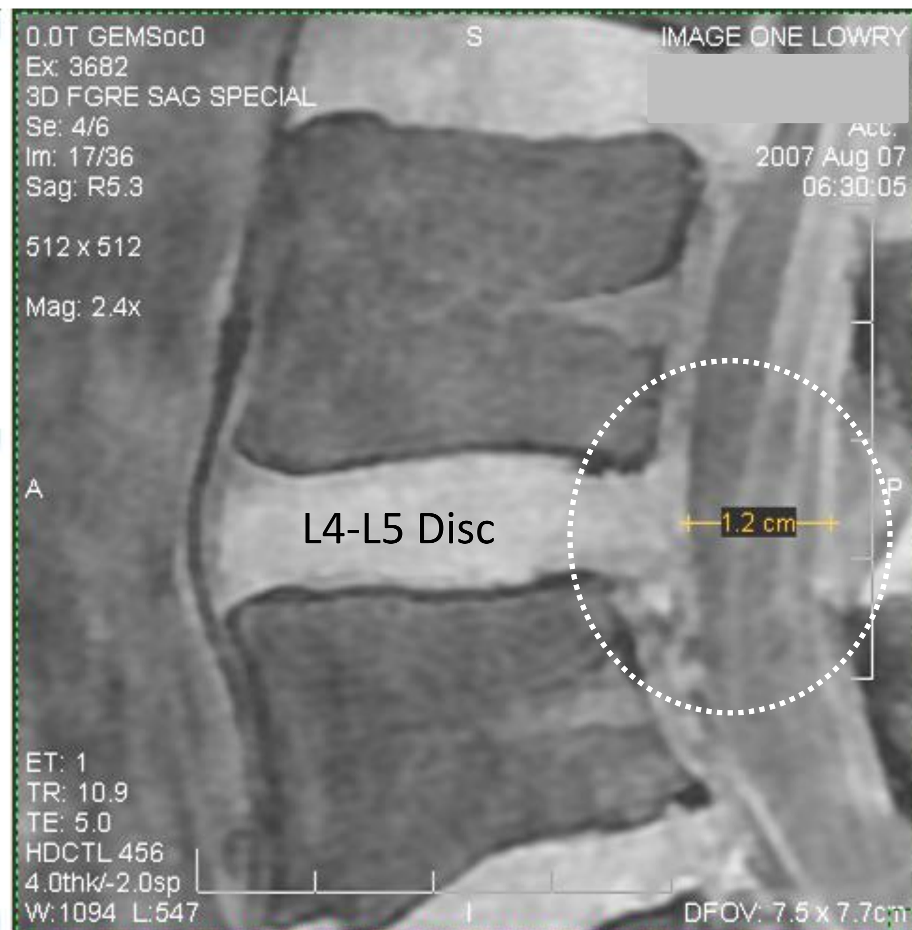

28 yo WF s/p failed microdiscectomy with several year history of low back pain and intermittent radiculopathy. 1 month post cell transplant on the left with 3 month post cell transplant on the right. Note the posterior disc bulge on the left has flattened on the right. Total canal diameter at this level has increased from 1.0 cm to 1.2 cm.

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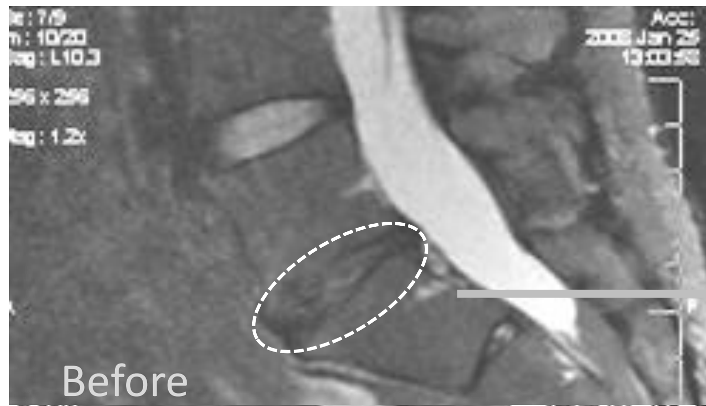
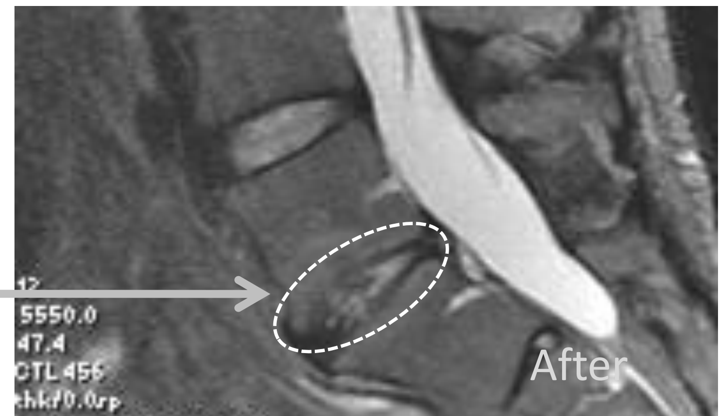
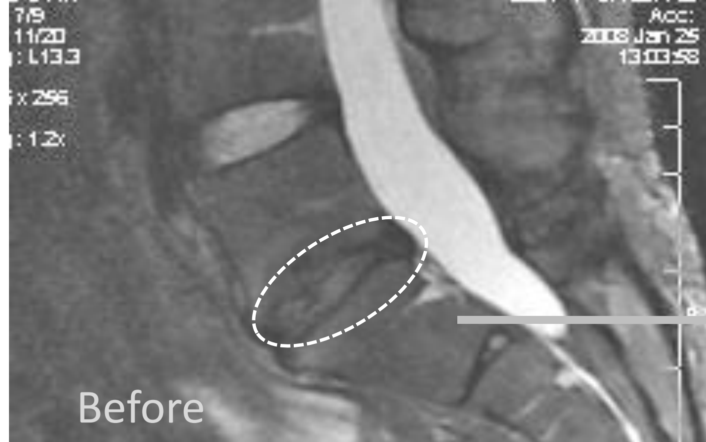
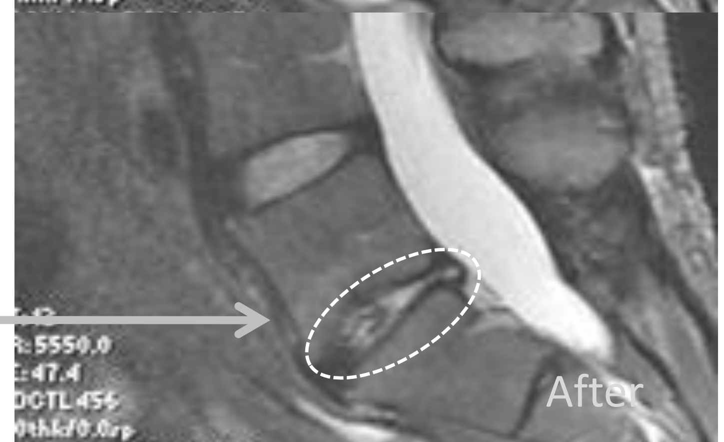
KG-39 yo WF-Pre-op Jan 08 Sag STIR 3.0T MRI with ET=12, TR=5550.0, TE=47.7



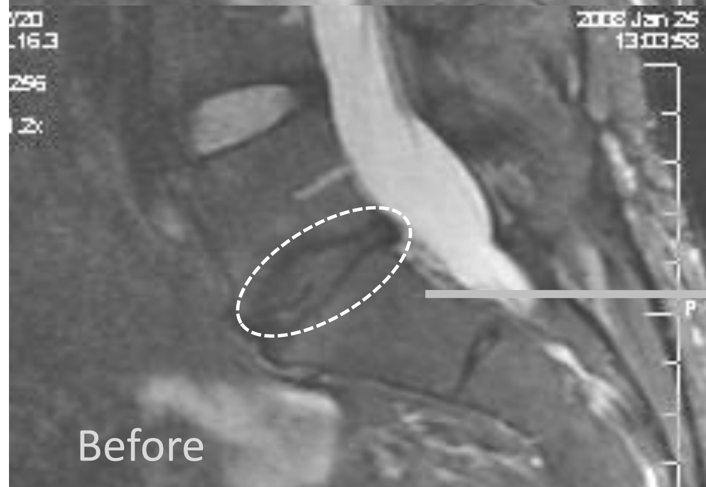


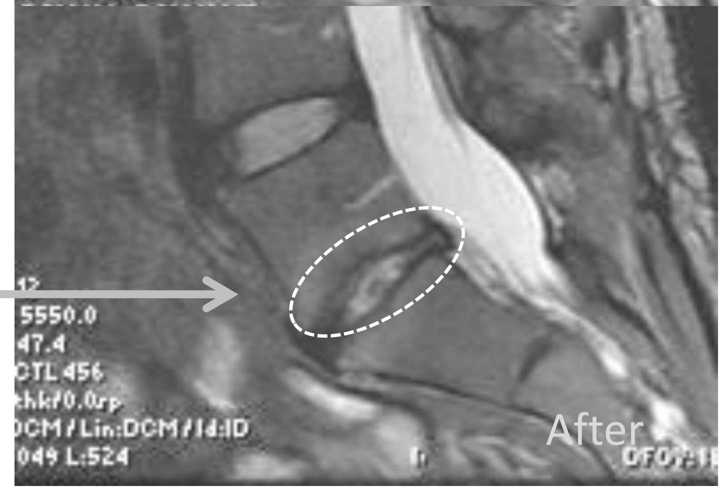
Post-op Feb 09 Sag STIR on same magnet with ET=12, TR=5550.0, TE=47.4

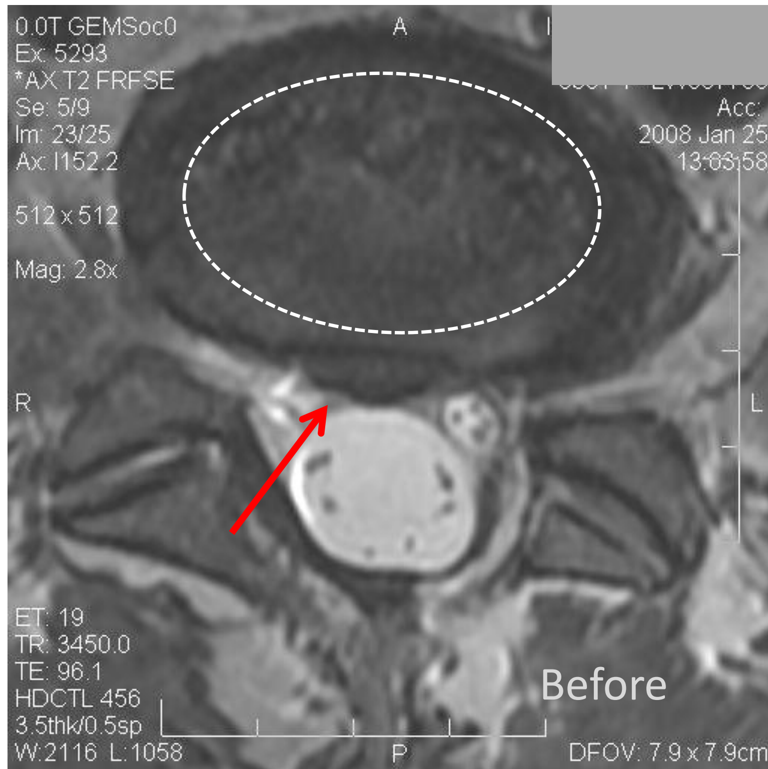


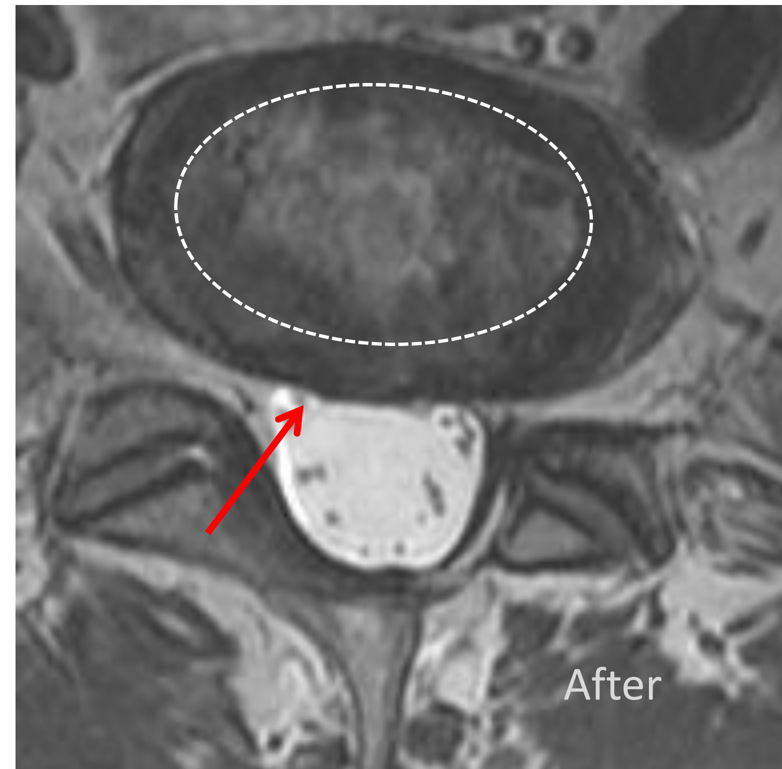


Note bright signal in nucleus pulposis of L5-S1 disc now more closely matches that of bright L4-L5 disc.









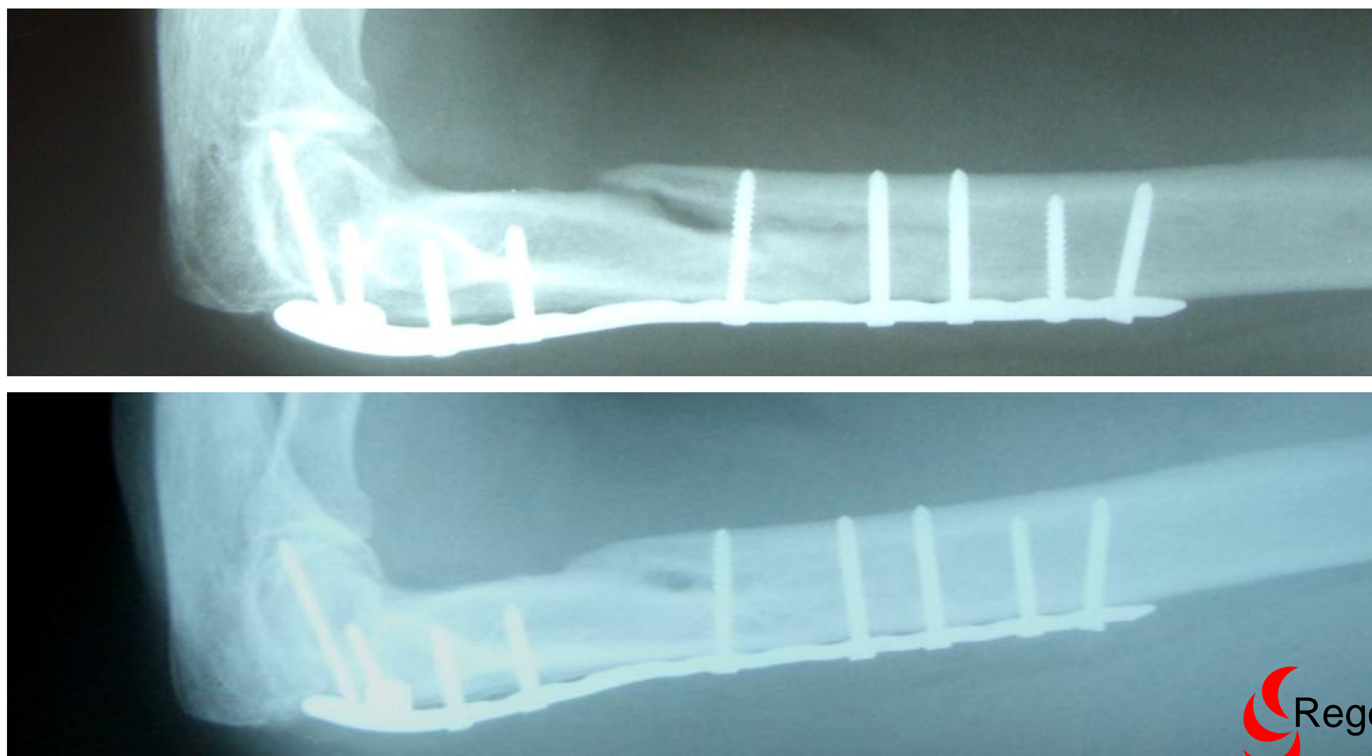
KG-Axial T2 FRFSE scans on the same 3.0T scanner. Note the increased T2 signal in the L5-S1 disc (brighter inside dashed circle) as well as the resolution of the right>left central disc bulge (red arrow).

Pre-op Jan 08: ET: 19, TR: 3450.0, TE: 96.1
Post op Feb 09: ET: 19, TR: 3450.0, TE:96.1

Full Thickness Rotator Cuff Tear in the Elderly

Angelina is a 78 yo WF with a degenerative/traumatic full thickness rotator cuff tear. After several months this had failed to heal. Since she had other medical problems and musculuoskeletal issues, it was decided that a non-surgical attempt at repair would make sense. What we didn't know was if we could expand her adult stem cells to the appropriate number or if such a degenerative full thickness tear in an elderly woman could be repaired using the Regenexx procedure. I have purposely darkened these images to try and help identify the high signal area of the tear. On the before image on the left, the dashed circle encloses an area of light color in the tendon. The after image on the right shows that this focal area of light color in the otherwise dark tendon is now not present. The patient reported increased activity levels and an ability to lift her arm again. At 6 month follow-up she had no shoulder pain and full active ROM. While this is not as much MRI change as we would expect to see in a younger patients with just a tear due to trauma, this does demonstrate that repairs of full thickness tears in the elderly can be performed using injection of cells rather than surgery. It should be noted that there was no immobilization of the shoulder with this injection.

38 yo WF smoker with a 9 month old non-union who had failed a trial of a bone stimulator. Cells implanted under fluoro into fracture lucency. After radiograph is 5 weeks after MSC transplant.



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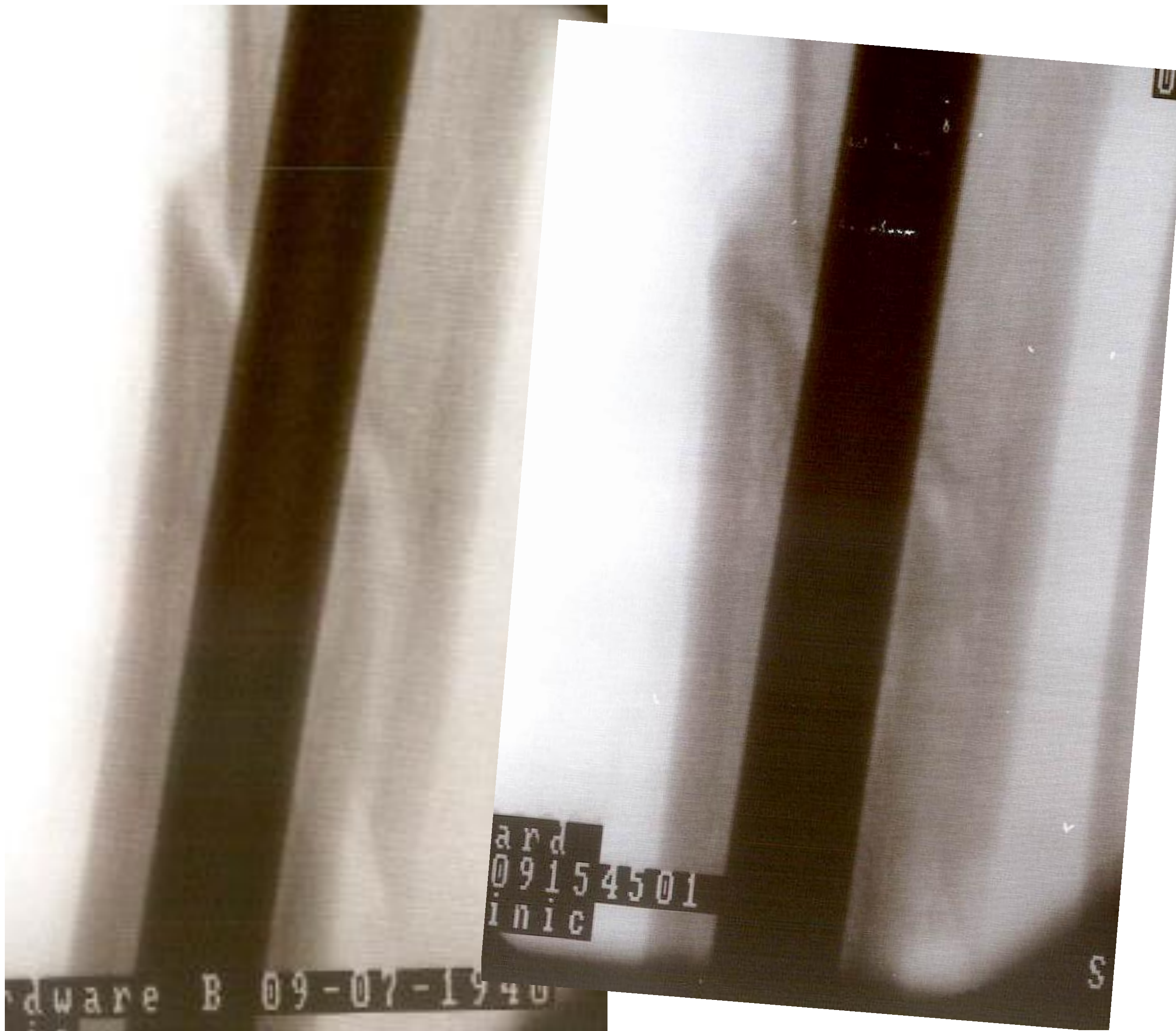
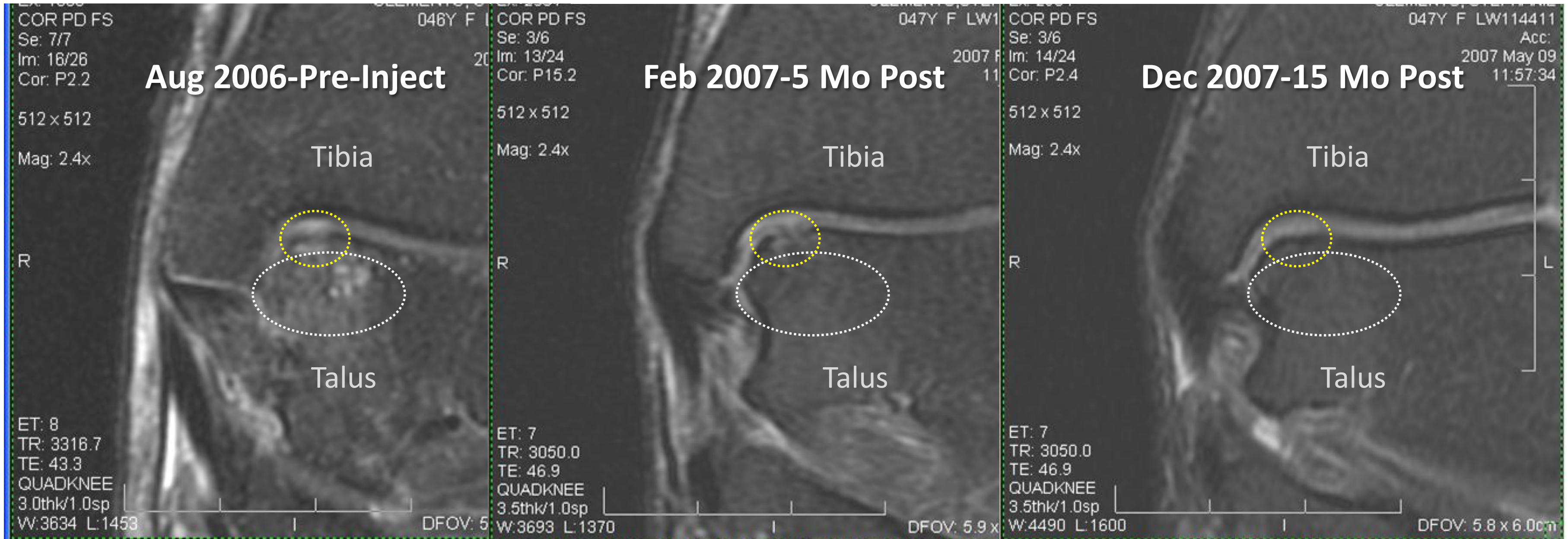


Before **5 Months After**

EW is a 67 yo WM with a 4 mo history of tib-fib non-union. The patient also has a history of osteoporosis as well as lumbar radiculopathy treated with epidurals and opiod pain management. He was offered an ORIF revision, but chose to have autologous MSC's re-injected into the fracture site using the Regenexx procedure. At 3 months post-procedure he reported 80% relief of pain and return to normal ambulation.

Regenexx



3.0 T Coronal PDFS serial MRI's of the same slice of the medial ankle/talar dome. These are pre-injection, 5 months post injection, and 15 months post-injection. Note again that the defect in the dark bony cortex line (seen as the "gap" in dark line in the Aug 2006 and Feb 2007 images-inside the yellow dashed circle) progresses to dark cortex by the Dec 2007 image.

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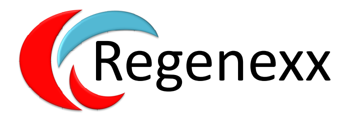
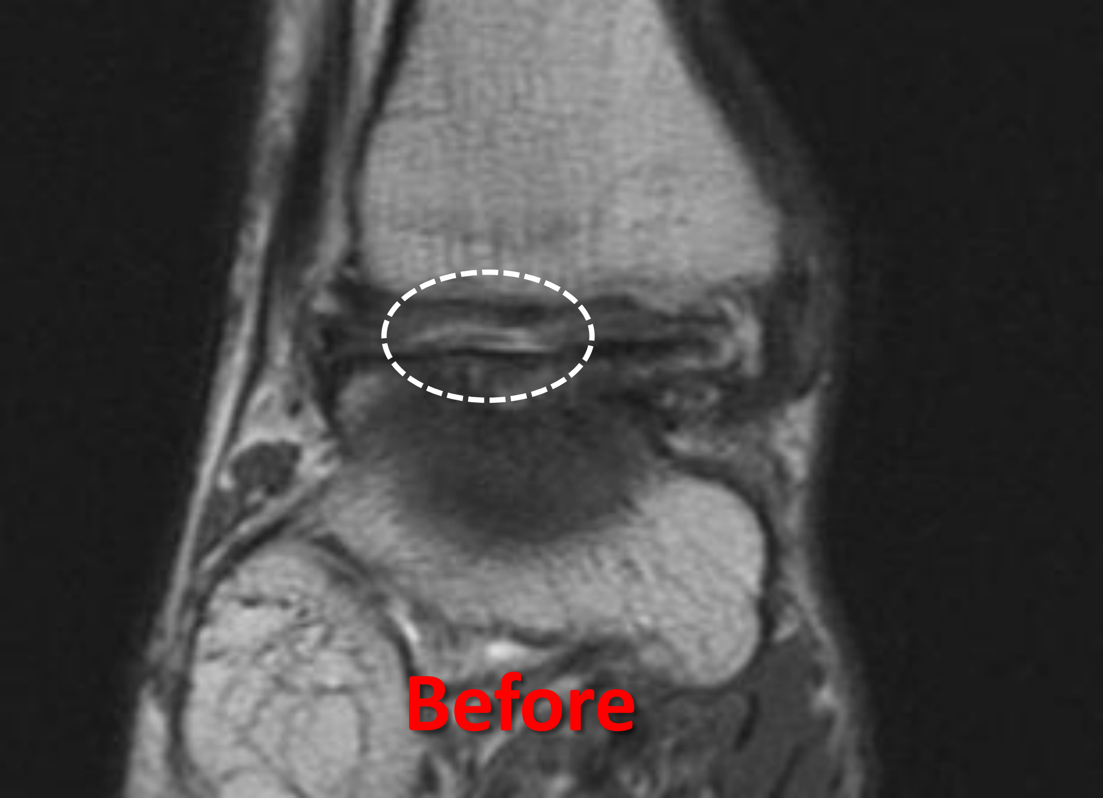
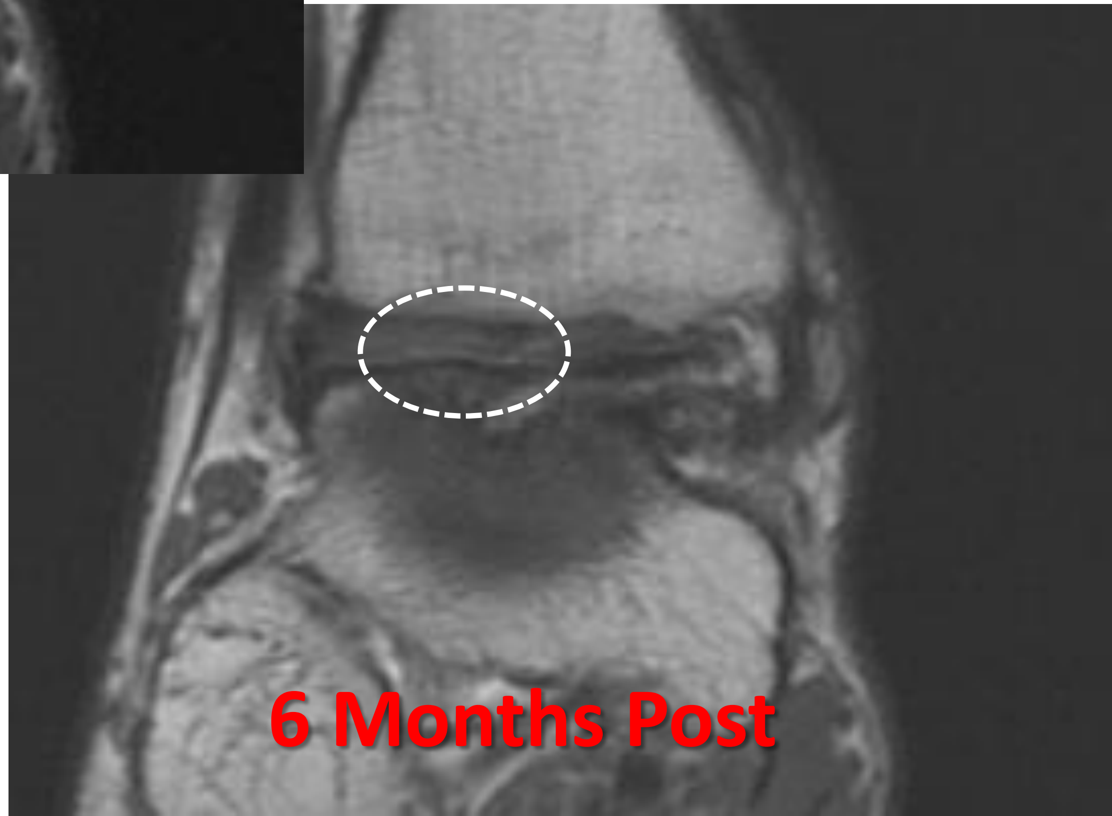


30 yo WM with a congenital absence of the fibula and a dysplastic foot with chronic pain in the talar dome region. The before images show an area of high signal that resolves 6 months after the Regenexx procedure.





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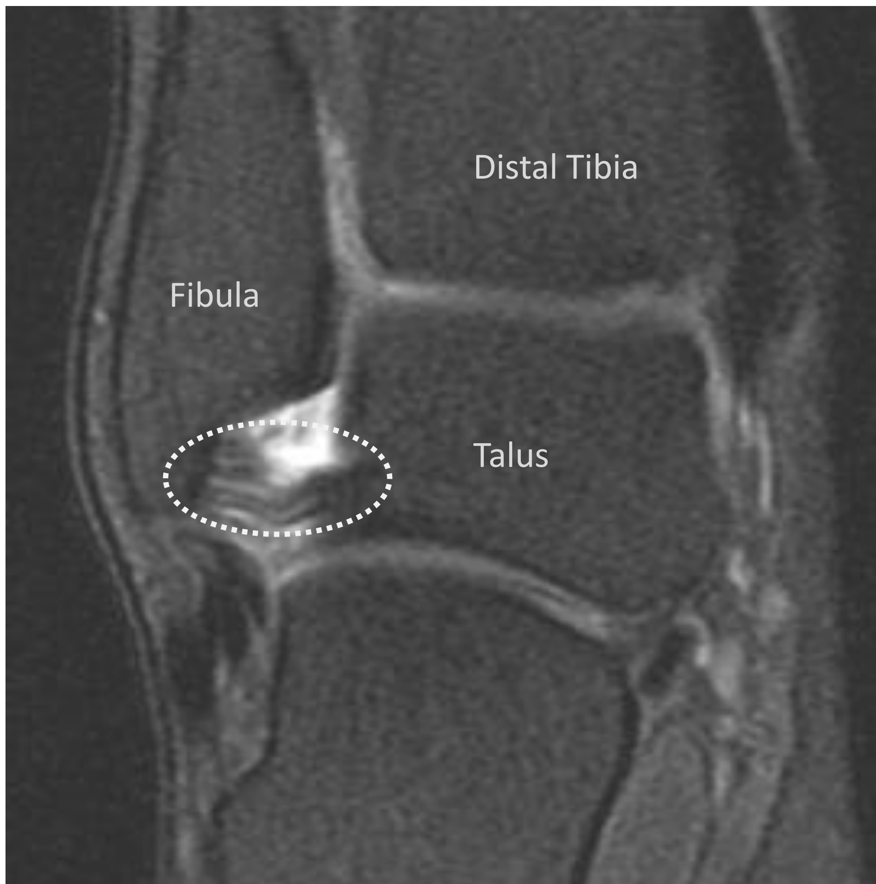
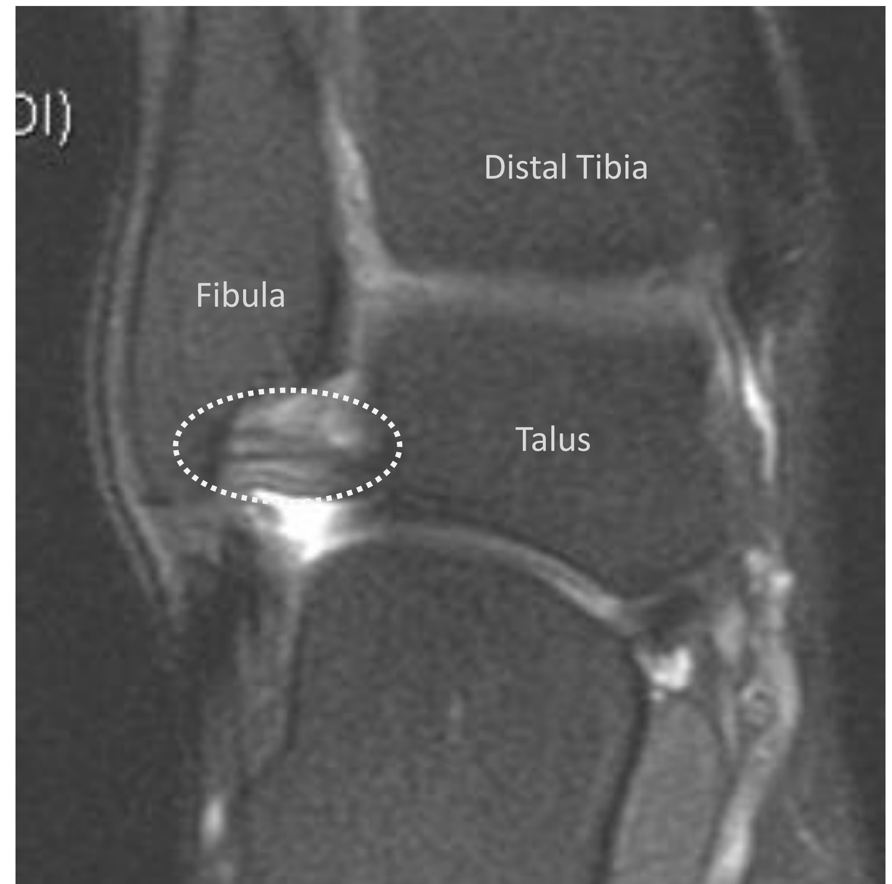
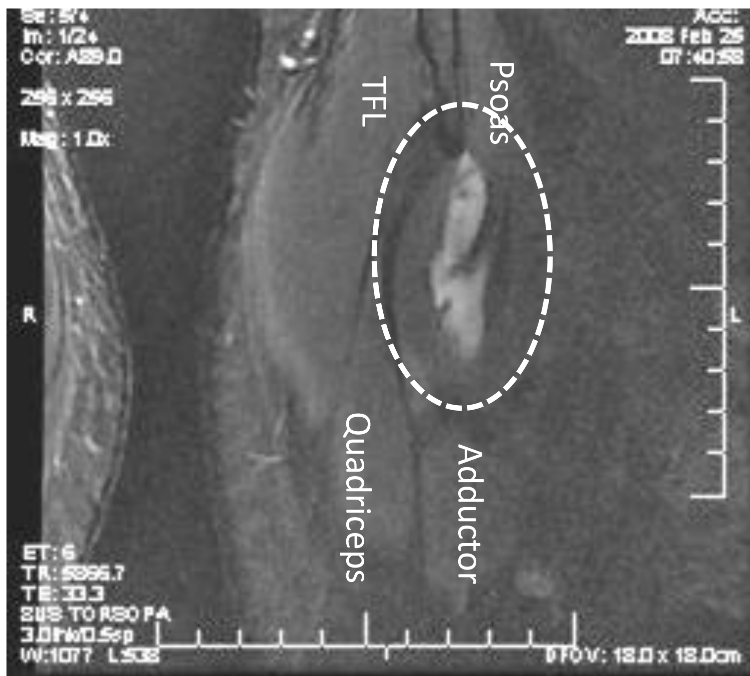


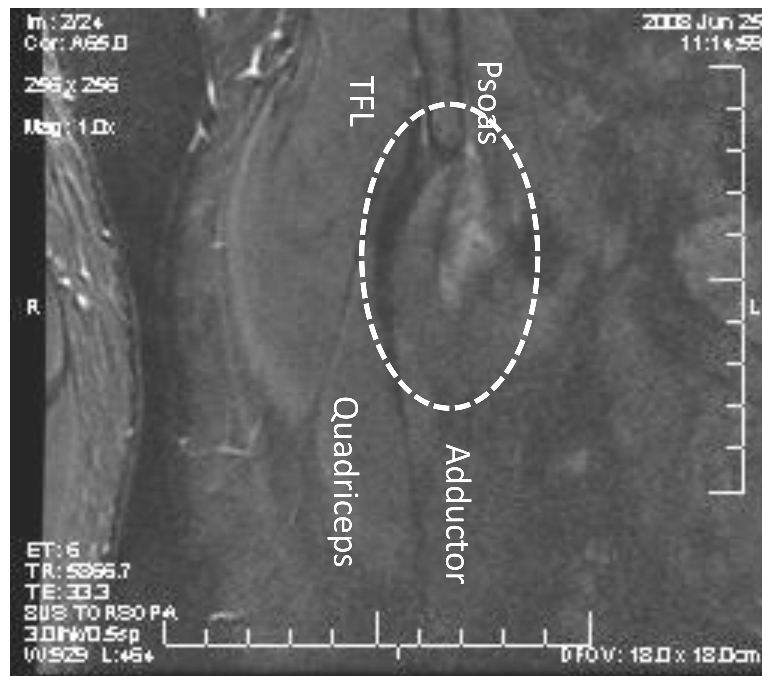


32 yo WF with a several year history of significant ankle pain from a fall. Pre and 3 month post MSC transplant COR PDFS 3.0T MRI of the lateral ankle ligaments and talar dome. The patient had failed arthroscopic debridement, steroids, prolotherapy, and physical therapy and still had chronic ankle pain. Note the partially disrupted talo-fibular ligament (in dotted white circle) on the left on the January, 2008 pre-op image. The same ligament in the May 2008 MRI shows that the upper portion of the ligament has repaired and that the "crimped" appearance of the sub failure stretch injury present in the left image has returned to the more normal morphology. The patient had complete resolution of lateral ankle pain and this procedure required no immobilization. For more information, e-mail centenooffice@centenoclinic.com.

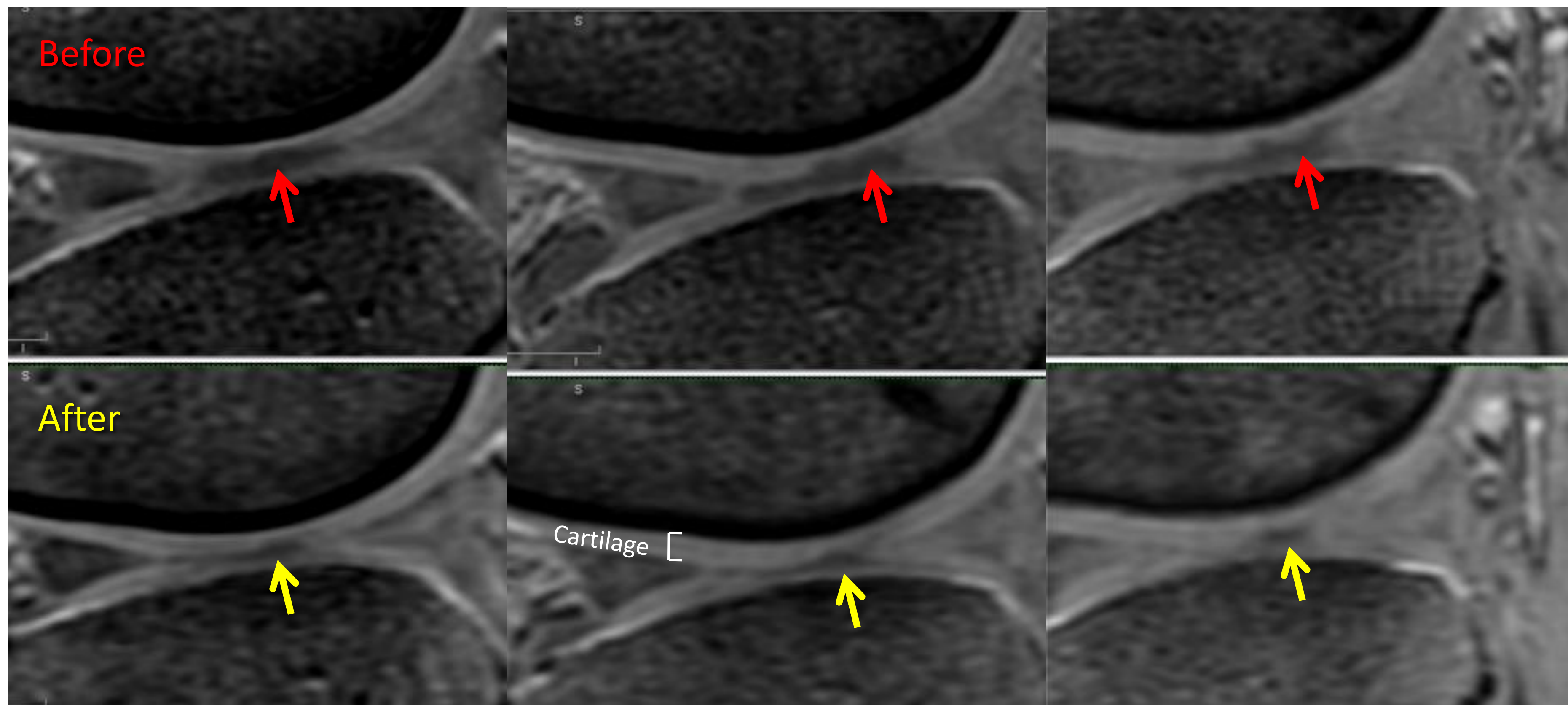
Regenexx

57 yo WF s/p gastric bypass with >1 year history of anterior hip pain. After failing steroid injections, she was told she needed a hip replacement. However, diagnostic blocks showed that her hip was not the main pain generator, but in fact most of her pain emanated from a swollen iliopsoas bursa. Bursa's are lubricating sacs that allow free movement often between muscles/tendons and the bony areas they pass over. The bursa is seen in the before image as the large whitish area in the dotted circle. She obtained only 1-2 weeks of relief from several x-ray guided corticosteroid injections into this area. The first attempt at obtaining MSC's and growing them in culture yielded few cells which only provided transient relief and little MRI change when injected into the bursa (likely due to malnutrition from the gastric bypass). The second attempt at cell isolation and culture proved more successful due to advances in culture techniques. The images are 3.0 T Coronal STIR's taken before and after the second injection of cells. The left shows a large whitish area in the dotted circle which represents the very swollen iliopsosas bursa. The right after image barely shows any white area, meaning the bursitis is mostly resolved. This is c/w her report of 80% improvement at 6 months post-procedure. It's important to note that she had already been offered a total hip replacement and that the only other way to deal with this chronically inflamed bursa would have been to remove it via open surgery.





BEFORE-FEB 2008 **AFTER-JUN 2008**



The white bracket outlines the cartilage layer in this Sagittal MRI. The red arrows point to the OCD (hole in the cartilage). The breaks in this layer are shown by the red arrows. The yellow arrows point to the defect one year after the Regenexx knee procedure. Note that the breaks are much less in the after image and for the most part have been "filled in".

Pi Gr- Top images are pre-op in Jan 07- 3D FSPGR Sag -ET=1, TR=9.4, TE=4.4. Bottom images are Jan 08- 3D FSPGR Sag -ET=1, TR=9.4, TE=4.4. Note significant reduction in size of OCD.

BEFORE

13 MO AFTER

Meniscus

34 yo WM with a history of complex medial meniscus tearing. Notice that the post-op films show consolidation of the vertical tearing (the darker color of the meniscus in the dashed white circles). The patient reported excellent relief. Of chronic medial knee pain with physical activity.

Proton Density Fast Spin Images with a 3.0 T MRI

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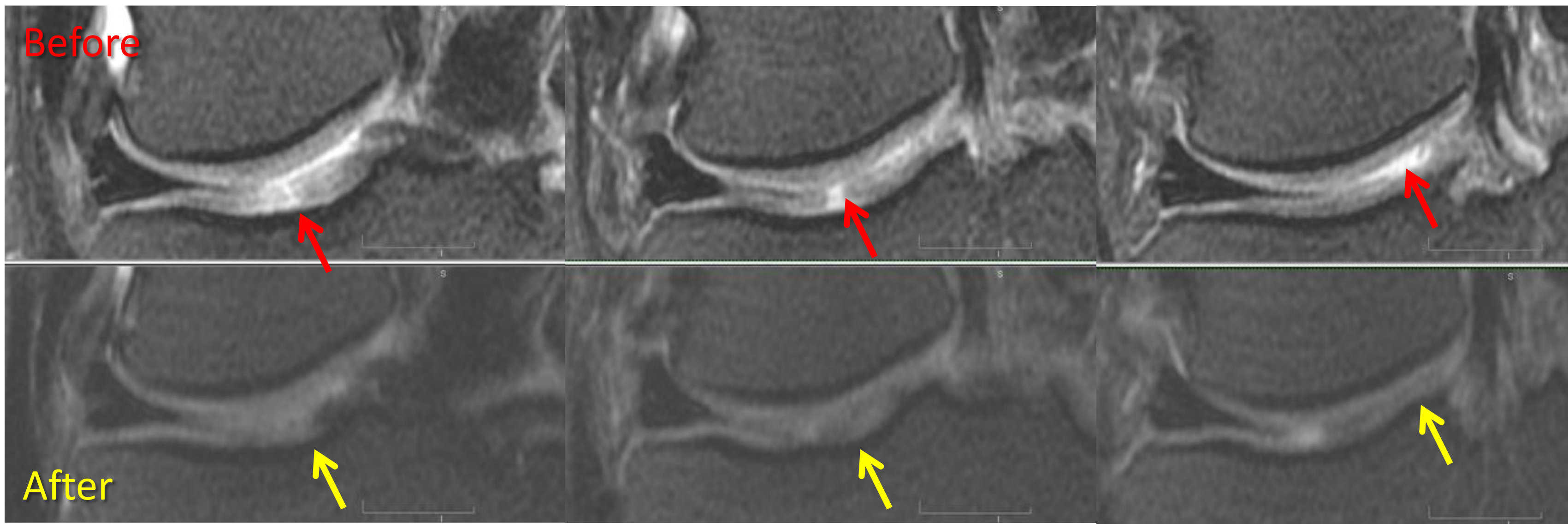
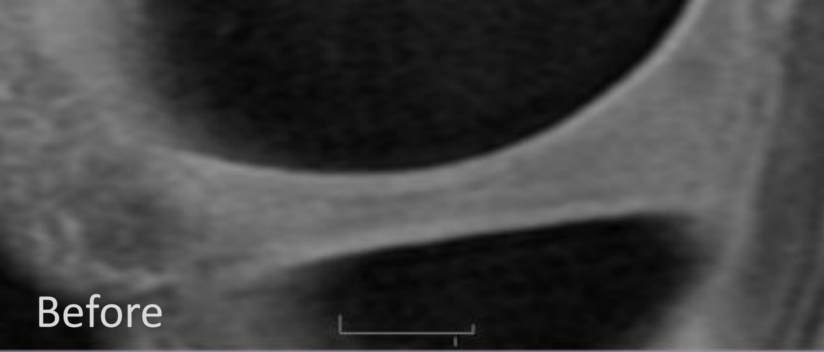
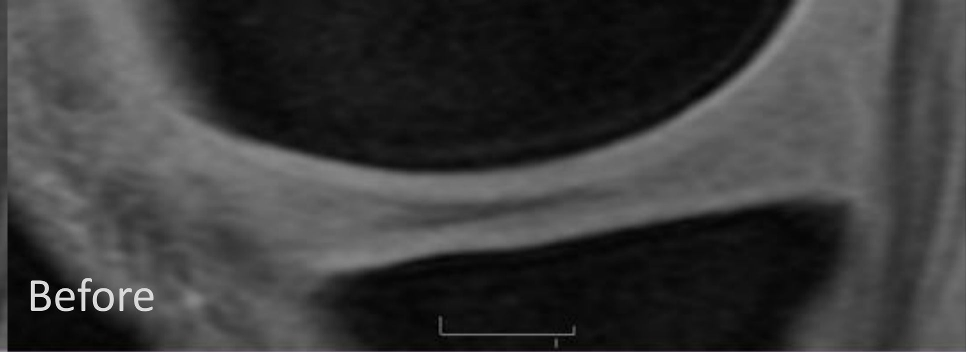
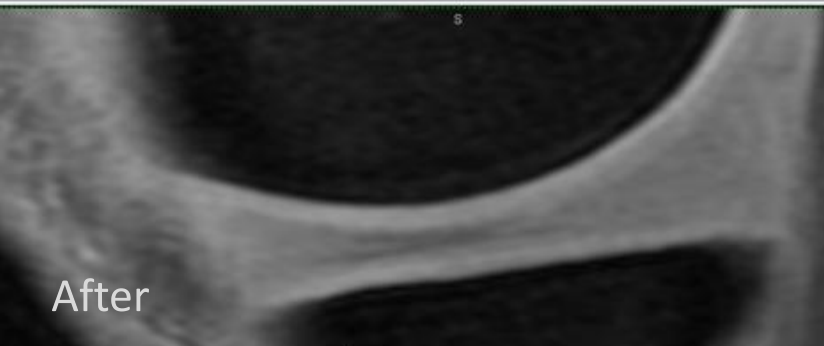


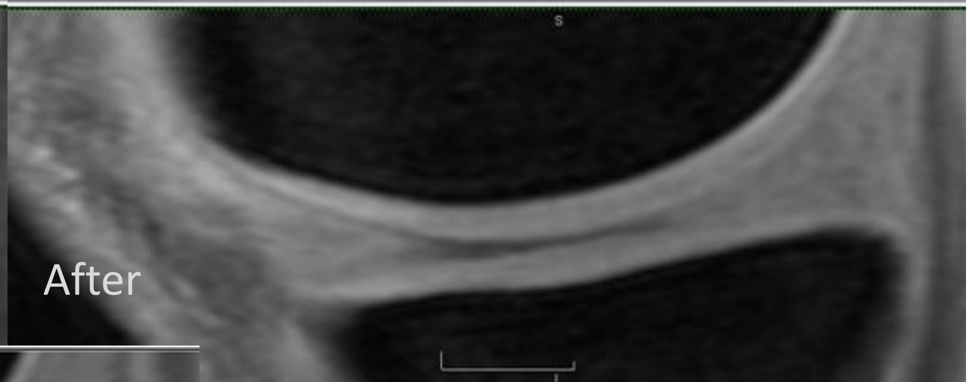
These images scan across the area of the knee with obvious defects in the grey cartilage on the darker bone. Note the red arrows on the "Before" images show breaks in the grey cartilage (whiter areas in the grey). The bottom images are 16 months after the Regenexx knee procedure. Note the yellow arrows point to the same areas which have now "filled in" with grey cartilage (no more white areas).

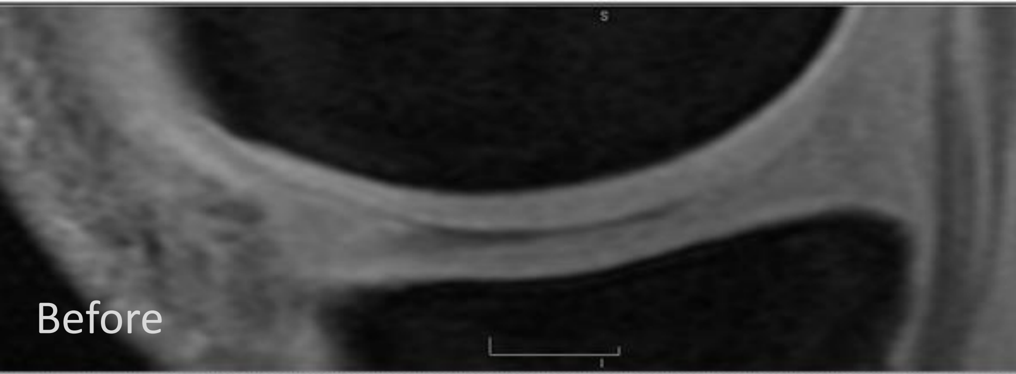
Ba Ja-51 yo WF-GE 3.0T MRI with COR PDFS-Aug 2007-Top images pre-op- ET:7, TR: 3150.0, TE=46.9. Bottom images post-op Dec 08- ET:7, TR: 3150.0, TE=46.9.

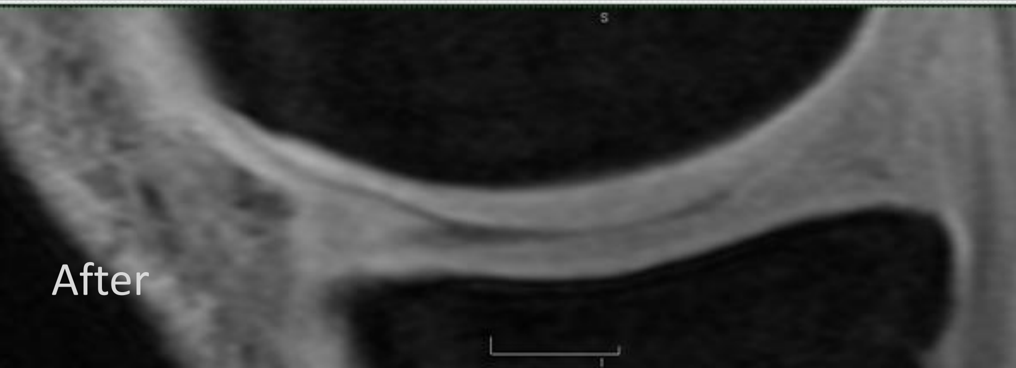






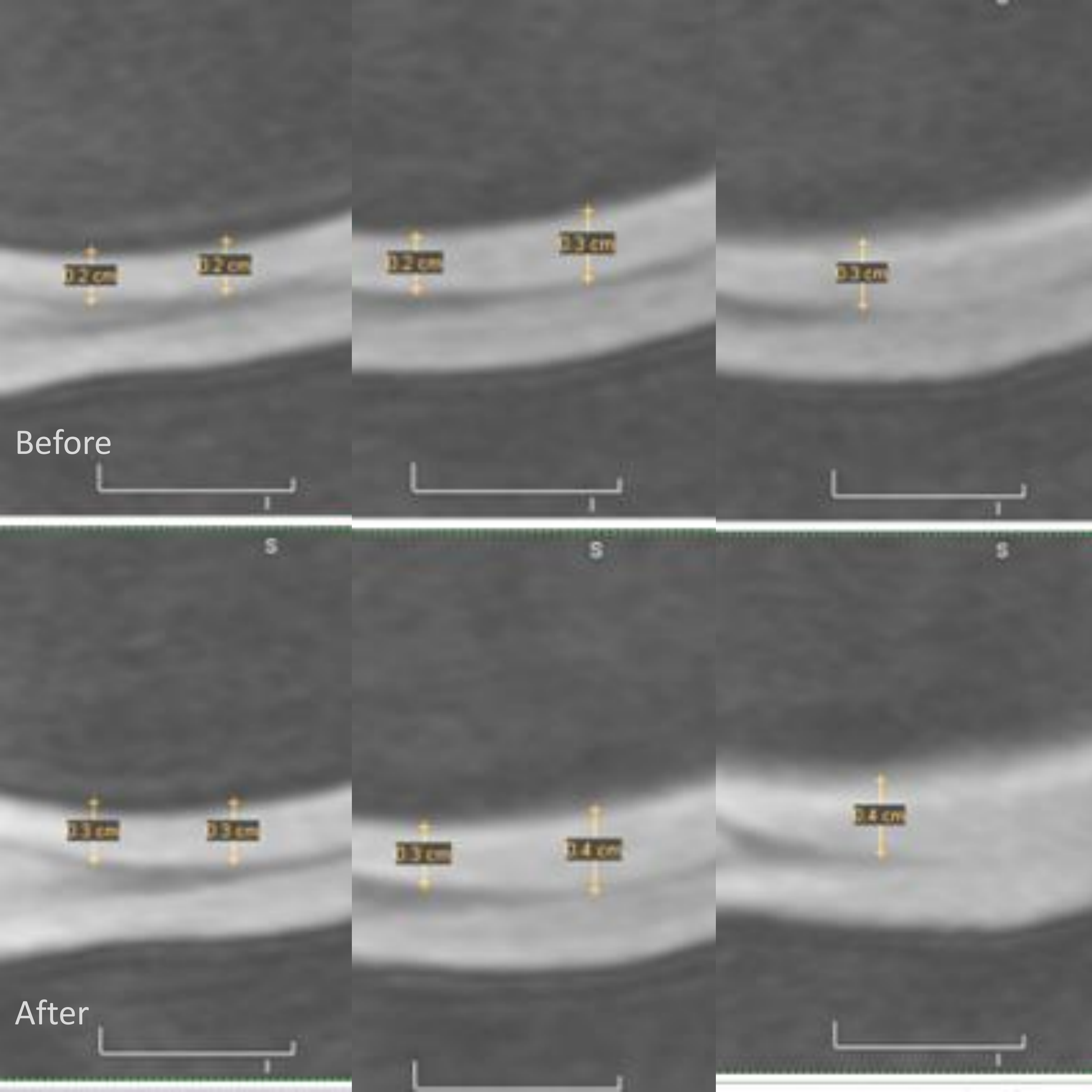






Patient Ch Na- 37 yo WM-Before image is 5 months post first MSC transplant. After is 3 months post 2nd MSC transplant.
3D FSPGR FS SAG of medial knee compartment.
Before: ET: 1, TR: 12.9, TE:2.1
After: ET: 1, TR: 14.0, TE: 2.1

Note thicker cartilage with brighter signal in bottom after images.

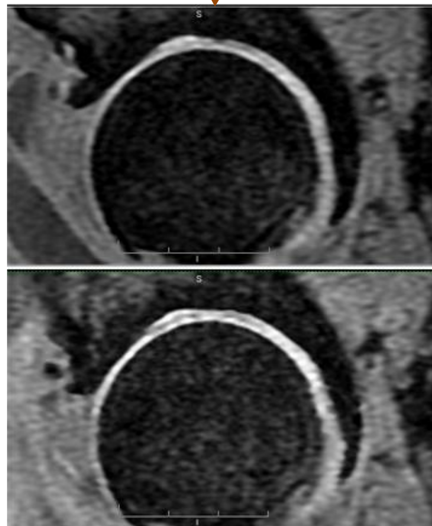


Same patient Ch Na- 37 yo WM-Before image is 5 months post first MSC transplant. After is 3 months post 2nd MSC transplant.
3D FSPGR FS SAG of medial knee compartment.
Before: ET: 1, TR: 12.9, TE:2.1
After: ET: 1, TR: 14.0, TE: 2.1

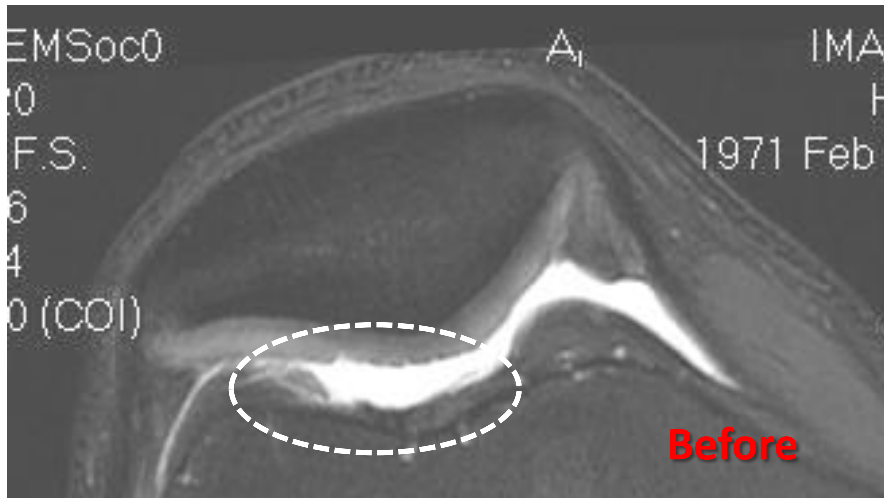
In same image slices as in prior page, note thicker chondral cartilage in bottom after images, generally 1 mm thicker (25-33% thicker) than before.

Before

6 Months Post



37 yo WM-3 months post 3 injections of autologous mesenchymal stem cells into the medial trochlear groove. 3.0T before and after axial PDFS sequences taken on different magnets.



Note appearance of cartilage in white dashed circle, before image shows ragged appearance with breaks on the patellar surface and the medial trochlear groove surface. The two best match axial slices on the right show improved contour of the cartilage with fill in of the defects.

Change in Meniscus and Cartilage Volume as Measured on 3.0 T MRI (3 consecutive patients)

*Note that the standard error measurement of three measurement trials was subtracted from the reported change in volume result.