Trends-in-Medicine

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By Lynne Peterson

SUMMARY

Artificial discs clearly stole the show. There was tremendous interest in discs, especially since the first artificial disc, Johnson & Johnson's Charité, was approved at the beginning of the meeting. Doctors predicted that an average of 19% of their fusion patients over the next year will get a Charité artificial disc instead, and they expect this to be driven by strong patient demand. ♦ Spine surgeons continue to favor kyphoplasty over vertebroplasty, but growth in kyphoplasty procedures is expected to slow due to cost, reimbursement, rumors CMS will change reimbursement with a new CPT code, and improving results with vertebroplasty. Kyphoplasty is good medicine, but it's bad from a business sense, doctors said. ♦ The high cost of the first BMP, Medtronic's InFuse, is limiting use, and excitement over BMPs in general appears to have waned a bit.

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Artificial lumbar and cervical discs, nuclear replacement devices, and dynamic stabilization were the key focuses at the 2004 North American Spine Society (NASS) meeting. However, fusion promoters (e.g., BMP) and vertebral fracture treatments (kyphoplasty and vertebroplasty) got a lot of attention. Spine surgeons also got an update on the reimbursement and litigation environment.

ARTIFICIAL DISCS

LUMBAR DISCS

Not surprisingly, Johnson & Johnson/Depuy's Charité lumbar disc replacement dominated this year's NASS meeting. The FDA approved Charité on the first day of the meeting (October 26, 2004), and the J&J booth was crammed with doctors looking for more information or trying to sign up for the mandatory training class. Every session on artificial discs was packed or overflowing, indicating strong interest on the part of doctors.

Are artificial discs just hype or are they the next "cage rage"? Sources generally agreed that there will be heavy patient demand for artificial discs.

- *Speaker:* "My personal prediction is that this will be patient-driven…I think they will peak in about Year 4, and then fall and find a reasonable level of use around 25% (of procedures)."
- *California:* "Part of the problem is this is patient-driven…Patients don't want a fusion. They want a disc replacement. The ones who truly need fusion and don't want it will shop around to find someone who will do a disc replacement and try to force the issue for a disc replacement because that is what has been conveyed to them as the best possible treatment. Part of the problem is there are no exact and strict indications."
- *Brazil:* "Patients are waiting for this…If you have a big pressure on surgeons to start more quickly than they are prepared to do, this can have some repercussions on complications. We know that 95% of the complications are related to access, not to the disc work itself."
- "Charité will be overused, the same as with cages…There will be press releases and anecdotal stories about how it 'saved my life when nothing else helped.' Everyone will want it and not realize it isn't a panacea for all back pain…People will start doing it who didn't do fusion…They will find that patient selection is difficult, and they won't know how to sort the patients out…So there will be an upsurge, overuse, and then use will fall back to a more reasonable level of use…The use in inappropriate patients will be bad for the company."

- *Nurse:* "Everyone wants disc replacement. Everyone is on the Internet…and they think preserving motion is the answer to everything …We spend a great deal of time explaining to patients that it has its place – but everyone wants it."

Artificial discs offer patients faster recovery, and that is a huge draw, doctors said. One commented, "The problem with fusion is you can't do certain things for three to six months, and by then the patient has lost the ability to get back to a normal lifestyle – maybe losing his job or house…patient satisfaction is heavily in favor of disc replacement…I frequently don't do (fusion) surgery on people who are working. I tell them to live with the pain." Another doctor said, "Patients are really enthusiastic (about artificial discs). The next day they can go home without any special restrictions, and in 15 days they can go to the swimming pool…With both lumbar and cervical discs they recover faster." A speaker added, "The transition period (for artificial discs) is more like 3-6 weeks instead of 3-6 months."

The long-term data from Europe on artificial disc products did not show any dramatic failures, and the lumbar disc data indicated Johnson & Johnson's Charité and Synthes' ProDisc hold up well over time. An expert said, "Out to 10 million cycles, there is less wear and debris than with hips or knees, so I don't expect the same issues. We haven't seen that in Europe."

After lumbar fusions, the data indicate that adjacent levels develop fractures in 2.7%-5.6% of patients. It is possible that disc replacements reduce the rate of adjacent fractures, but this is still controversial. Complication rates are about the same for fusion and disc replacement.

The data appear to indicate that pain and disability outcomes with lumbar fusion and lumbar disc arthroplasty are equivalent after six months. However, patient satisfaction appears to be much higher with disc replacements than fusion.

Patient Satisfaction with Spine Procedures

Procedure	Patient satisfaction range
Lumbar disc arthroplasty	66% - 90%
ALIF	65% - 93%
Circumferential fusion	80% - 90%
Posterior interbody fusion	85% - 90%

Key Lumbar Discs in Development

Issue	Charité	ProDisc	Maverick	FlexiCore
Company	Johnson & Johnson	Synthes	Medtronic	Stryker
Material	Metal-on-poly	Metal –on– polyethylene	Metal-on-metal	Metal-on-metal
Status	FDA approved 10-26-2004	FDA approval expected in 2005	IDE completed June 2004	IDE about to complete enrollment (2-year follow-up)
Axial rotation	---	Constrained	Constrained	Constrained
Rotation	---	Unconstrained	Unconstrained	Semi-constrained
Lateral bending	---	Semi-constrained	Semi-constrained	Semi-constrained
Flexion/extension	---	Semi-constrained	Semi-constrained	Semi-constrained
COR	In center	---	In posterior 1/3 of device	---
Core	Unconstrained	---	Semi-constrained	---
Design	Smooth endplates	---	HA coating, keeled	---
Complications	18.8% in training 16.2% in study 2.3% in continued access 10.7% overall	---	---	---
Overall patient satisfaction	64%	---	---	---

Several interesting points were made during a discussion group on artificial discs:

- Doctors urged J&J/Depuy to control which doctors are permitted to perform disc arthroplasty with Charité. One said, "Depuy needs to stay on the high road – to make sure that people who get in the (training) course should be in the course." A J&J official responded that it isn't J&J's place to control who performs the procedure, "Obviously, our role as a manufacturer is not to practice medicine or regulate it, but to provide information, educate on products, educate on the use of products, and make sure that is clearly communicated. Our role is not to go beyond that and regulate what doctors think is in the best interests of patients."
- "We have an access surgeon who has done it for 11 years…but it has to be exactly in the center…Even with my great access surgeon, it is sometimes radiologically hard to see the center. Sometimes when you think you are in the center you really are off a little."
- Patient selection is very important.

Advantages to Lumbar Disc Replacement

Advantages
Less operating time
Less blood loss
Shorter hospital stay
No graft-site problems
No pseudoarthrosis
Single levels do better than multilevels
Patients with no prior surgery do better than those with prior surgery
May prevent adjacent segment disease

JOHNSON & JOHNSON'S Charité

Key take-away messages from NASS on Charité included:

➢ **Launch outlook.** Orthopedic surgeons and neuro-surgeons who were interviewed estimated that an average of 15%-25% of their fusion patients over the next year will get a Charité artificial disc instead. Even doctors who said they are not ready to leap into Charité generally admitted that from 5%-15% of their fusions over the next year probably will be Charité instead – because of patient demand.

The fusion cases that will be impacted most are younger patients (<50) with single level disease, most of whom would otherwise have gotten a fusion with BMP, sources said.

Spine surgeons commented about Charité and estimated the percent of their fusion procedures that will be done with an artificial disc during the next 12 months (% in parentheses):

- *Missouri #1* (20%): "I'll use Charité in patients with documented disc pain and negative facet degeneration. This will be mostly young patients – under 40 – with isolated disease. I will only do single level…I won't lose money, but I won't make as much."
- *Missouri #2* (25%-50%): "We do a lot of two and three level fusions. I'll start with single level, but I want to get into the multilevel study."
- *Virginia* (25%): "There is little downside to Charité…It is not hard to do for a good spine surgeon...Patients will demand it, and more will be done than should be done…I wouldn't start with multilevel or terrible arthritis…This is not a Medicare patient population anyway. You have to exclude patients with posterior disease and avoid doing it in patients with horrible facets…I've seen a lot of things come and go, but I think this will find a place."
- *Ohio* (0%): "I want more data before I use Charité. I was not aware of the European data. But I probably will get trained, and I may do some because you can always go to fusion later."
- *South Carolina neurosurgeon* (15%-20%): "I won't start with multilevel, but I'll be doing them within a year…Charité probably won't be available in our area for a couple of months, so I'll probably start in March 2005."
- *Texas* (<5%): "I will get training and do it, but not often because a lot of third party payers won't pay for it with a tracking code. That is a problem."
- *Florida* (5%-10%): "I've already had patients ask for it. First, I'll watch what others do, and I'll start with single level only. Reimbursement is not an issue. Everyone will jump on the (Charité) bandwagon, and new problems will come up that weren't seen in the trials because those were ideal patients."
- *Michigan* (<10%): "I will get trained. I've been waiting for it since 1997. But I'll only do single level at first."
- *Texas* (50%): About 10% of spines are unstable and so artificial discs are contraindicated, but I'm not sure bad facets are a good contraindication. I won't do any fusions any more. I'll send those to others and concentrate on artificial discs."
- *Nebraska:* "I haven't sorted it out yet. I'm interested in it. It is exciting, but it hasn't proven better than fusion yet. I'm reluctant."

➢ **Training classes.** Johnson & Johnson is taking an approach to the Charité launch that a J&J official described as "responsible adoption." The FDA has required that physicians take a J&J training course before they can buy or implant Charité. That course will only be taught in Cincinnati at J&J's Ethicon/Endo Disc Arthroplasty Institute. Each class is one day of didactics plus one day of a wet lab. If the doctor also wants to be trained on access surgery, there is an additional third day before the didactic class. Classes run Monday through Friday (not weekends), usually every other week, with from 25-40 doctors trained in each class.

This is not a first-come, first-serve sign up. J&J is identifying doctors with ALIF experience and higher volumes; these are the doctors who will be trained first so they can become secondary centers, where doctors who have taken the training course can go to observe additional cases. There is no sign-up sheet yet for these classes; signup will not begin for a "couple of weeks."

J&J officials indicated there are 2,500 U.S. spine surgeons who do complex procedures, and the company expects to have everyone interested trained within a year, with 60% trained within six months. Thus, adoption trends should be pretty clear in the second quarter of 2005, and 2Q05 should be the key to gauging the growth of this product. Sales growth could slow in 3Q05.

➢ **Reimbursement.** Reimbursement does not appear to be much of a barrier to adoption of Charité or other artificial discs. The pricing will vary across the country, and a J&J official said, "The local price will be comparable to a stand alone ALIF with a threaded fusion cage." Hospital pricing will also be related to volume.

Physicians will have a CPT Category 3 tracking code for arthroplasty, which apparently is sufficient at this point. Medicare device reimbursement for hospitals is a different story. There will be a significant gap between what Medicare pays under the discectomy DRG and the cost of Charité ($11,500). However, Charité is approved for patients aged 18-60, and doctors expect to put it in mostly younger patients (<age 50). Several sources explained that most Medicare-age patients have too much facet degeneration to be appropriate candidates for an artificial disc. Thus, Charité is not labeled for Medicare patients, it is not being marketed for Medicare patients, and doctors do not want to use it for more than the

rare Medicare patient, for whom they expect their hospital will pick up the "gap" between cost and Medicare reimbursement.

Physician's View of Cost Comparison

Item	ALIF	Fusion	Charité
Cage or disc	$6,000	$6,000	$11,500
BMP	$5,000	$5,000	0
Surgeon	$3,000	$6,000	$6,000
Hospital	$4,000	$8,000	$5,000
Operating room	$2,000	$4,000	$2,000
TOTAL	**$20,000**	**$29,000**	**$24,500**

➢ **Long-term data.** Two-year follow-up in the randomized clinical trial of Charité of 375 patients at 15 centers found procedure time improved and complications decreased with experience (>15 cases).

Measurement	High volume site	Low volume site
Average procedure time	98 minutes	127 minutes
Hospitalization	3.5 days	4.5 days
Neurological complications	4.5%	14.1%
Revisions	0.9%	4.7%

➢ **Types of procedures.** Doctors are likely to start with single-level use of Charité, but they may quickly move to doing multilevel procedures off-label even though the company and its investigators are not recommending that. A speaker said, "There is extensive two-level experience outside the U.S. The FDA regulates the promotion of a product, not the practice of medicine, but we haven't looked at the learning curve in that (multilevel). As part of training protocol we will advise new users to only do single levels."

One source cited a study suggesting that it is not important how the facets look. So, some – but not most – doctors may consider Charité for patients with facet changes.

➢ **Future.** Going forward J&J has plans for:

- An IDE study.
- A full PMA application for multilevel procedures, since about 50% of fusions currently are multilevel. A doctor indicated that an investigator-sponsored study will also be started off-label of multilevel procedures.
- Physician training plus web-based education and consultation.
- Defining surgeon attitudes.
- Five-year follow-up.
- A registry for new implants. An official said this is in the process of being developed.
- Engaging professional societies. An official said, "NASS is taking the lead in setting some emerging technology training recommendations…We are also working with AANS (American Association of Neurological Surgeons)."
- Raising the bar on study design.
- Submitting a supplemental filing to the FDA for a porous coating version, which is what is used in Europe. However, a spine surgeon noted that the procedure may be more reversible without a porous coating.

J&J officials and Charité investigators are extremely enthusiastic about this device. Among their comments were:

- *Charité investigator:* "On the first post-op visit, the receptionist knows who got a lumbar fusion or a Charité when they walk into the office. It is that dramatic…Many Charité patients have achieved a high level of function unusual for fusion patients – including four full term births, mountain climbing and rappelling, and very active sports. They come back with a zero VAS and normal OSWESTRY scores that I'm just not used to seeing in fusion patients. In the patients meeting the entrance criteria, it is my personal choice…If you choose the right patients and do the right surgery, you get very good results. We don't want to repeat the 'cage rage.'…It is my treatment of choice, and it has really revitalized my practice – and patients seem far happier than fusion patients."

- *Another Charité investigator:* "The key in the beginning is responsible use, and that means following the protocol. There will be expanded uses, but we need to do that in a controlled manner. We don't want 'cage rage' or a pedicle screw fiasco. We want this to be successful."

- *German doctor:* "Indications and patients selection are more critical than the device. Size and positioning are important…Precision (with this) is much more demanding than for any fusion device…Ninety-eight percent of complications are surgeon-related and not device-related."

Doctors had a lot of questions about Charité, including:

What will happen when Charité patients age and become osteoporotic?
An investigator said, "We don't know. My gut feeling is that there will be remodeling and a solid bony endplate, but it is possible they may impact into the endplate when the patient is 70 or 80."

Is there late subsidence?
The inventor of Charité said, "No. I have only seen migration – and that was with the older model."

Is there wear debris or any problem with osteolysis or giant body reaction?
An investigator said, "There are a couple of anecdotal patients where the device was irradiated in air. Now, it is gamma

sterilized in inert nitrogen gas. So far, there have been no cases of osteolysis…There is one notorious case from Australia and a few anecdotal cases from the Netherlands." Another expert said, "The wear debris with hips and knees is very different from this. This is not the same…It is quite a bit less than knees."

What do you do if the device fails?
An expert said, "(One study) found five revisions, which was a 2.4% revision rate at seven years. The FDA came to a similar figure. I'm seeing much less revision in my disc patients than the fusion group…You can revise these patients…With the right patient selection, and if you leave the anterior spine in pristine condition, then you can do revisions with fusion and still get a satisfactory outcome. My biggest advice is to watch patient selection and indications, and if you do that, it is extremely rewarding."

What do you do if the (surgical) site gets infected?
An expert said, "We didn't have any infections." Another expert said, "We've been doing anterior surgery for years with more than 4,000 cases, and we've had only one infection. The anterior lumbar space is very friendly for us. You have to be meticulous, but it is an area that is very forgiving."

How robust is the device?
A New Zealand doctor said, "My concern was active young patients…But I had a patient who is a police PT instructor. She was riding a bicycle and was knocked off by a truck…She was hit and her rib fractured, but the disc was fine." A Texas doctor said, "I had a 35-year-old snowboarder come in for six-month follow-up in a full leg cast because of a fracture above the knee for snowboarding. His back is fine."

How serious are retrograde ejections?
One doctor said he won't use Charité in young men because of this, but a Charité investigator said, "You have to counsel these patients. You have to tell patients that there is a 98.5% chance of not having this, and if they do get it, there's a 50% chance of it getting better. And the sperm is still good; they can still have children through artificial insemination."

Competitors were trying – generally without much success – to dampen enthusiasm for Charité. Among their arguments were:

- **Failures.** The devices will ultimately fail, and there is no good exit strategy when they do.
- **Adjacent fractures.** The incidence and impact of adjacent disc disease/fractures is unknown.
- **Shorter recuperation times are not worth the additional cost.** A speaker said, "(Charité) patients recuperate in half the time of fusion. How important is that? If the results were the same, then, of course, patients will choose the faster recuperation. But there is no data that artificial discs are safer than fusion…The big impact is that patients are much happier, but we can't take that too much…We can't base all decisions on patient satisfaction…I think there is a group that will benefit from artificial discs, but there will still be a role for fusion and other treatments."
- **Multiple levels.** Some doctors are already talking about doing multiple levels and extreme cases. A German doctor said he did a five-level case and put Charité in a patient with scoliosis. A U.S. doctor said, "We are getting two messages out of this meeting: (1) Be careful with this prosthesis; it needs to be controlled, and (2) Five-level disease and scoliosis can be treated. That is a very mixed message, and I'm not all that comfortable with that…I don't think this is the time to be advocating that."
- **Cost-effectiveness.** This hasn't been shown yet for artificial discs in general or Charité in particular.
- **Efficacy.** The FDA 510K approval process doesn't always guarantee the efficacy of a product.
- **Reimbursement.** This may be difficult. Charité has been designated a CPT Category III device. A reimbursement specialist said, "These are a new category…They are not valued by RUC, so you need to talk to insurers about their payment policy…They do facilitate data collection and claim submission, encourage a national reimbursement policy, and speed the code development process."

Hospitals also may balk at covering Charité or other artificial discs if they are going to lose money. Charité is priced at $11,500 list. For 2005 Medicare will pay for total disc arthroplasty this way: $6,253 for DRG499, and $4,113 for DRG500.

Several doctors at one session said they do not plan to argue with insurance companies to get procedures covered. One commented, "I would wait for more data before I can go to an insurance company and say, 'Look, with this data, it is justifiable.' I don't think we are there yet." Another doctor said, "Remember, having a CPT code doesn't mean you will get paid…CMS said payment for services in Category III are at the discretion of local carriers…(Category III codes) are effective, more specific, more functional versions of unlisted codes."

- **Non-spine surgeons implanting artificial discs.**

SYNTHES ProDisc

The IDE for ProDisc began in October 2001 and covered 1-2 adjacent levels from L3-S1. The ongoing, prospective, randomized clinical trial is comparing ProDisc to 360° fusion (an FDA-mandated comparator). A researcher from the Texas Back Institute reported on 1-2 year follow-up data on 225 patients operated on so far. It was clear that patients had shorter procedure times, shorter hospital stays, faster recovery, and quicker return to work.

However, there were seven cases that required repeat surgery and one DVT with ProDisc. These repeat cases included a burst fracture at L5 in a 2-level case. An investigator said, "We don't believe this is related to keel design. This was a patient who was osteoporotic…We did not require patients (in the trial) to receive BMD evaluations unless they were postmenopausal females. This patient had not gone through menopause, but in retrospect she did have osteoporotic bone. The bone was soft, the implant was placed, and at six days she developed a fracture and required revision. The implant was removed, and she had fusion…So, the conclusion is we should fully evaluate patients for osteoporosis…Now, we do BMD on almost all of our patients before surgery, even males."

1- and 2-Year Results of ProDisc

Measurement	ProDisc n=187	Fusion n=38	p-value
L level	81 patients	17 patients	---
2 level	39 patients	16 patients	---
Mean operating time	230 minutes	75 minutes	<.001
Length of hospital stay	2.0 days	3.3 days	<.01
Return to work	8.4 weeks	15.6 weeks	---
Return to full duty	10.6 weeks	16.3 weeks	--
Need for additional surgery	Higher with ProDisc		---
Efficacy at 6 months			
Flexion/extension	Up 6.0	Down 2.5	---
Side bending	Up 3.4	Up 0.6	---
VAS scores	Better at every time point with ProDisc		<.05
OSWESTRY scores	Better at every time point with ProDisc		<.05

The ProDisc data presentation also was criticized for including compassionate use and continued access patients as well as trial patients. However, a source said Synthes is required by the FDA to include all these patients in its result reporting.

Data from 78 patients at one site in the ProDisc multicenter, prospective, randomized clinical trial indicated the VAS disability score and the OSWESTRY score both showed earlier improvement with ProDisc vs. fusion, but the scores were very similar by 18-24 months. However, patient pain satisfaction at 18-24 months was much higher with ProDisc; 94% of ProDisc patients said they would do the surgery again vs. 57% of fusion patients.

CERVICAL DISCS

There was less discussion of cervical discs than lumbar discs at the meeting, but doctors were aware that cervical discs also are on the horizon. A South African doctor who already is using them commented, "We've had this technology for five years…It will be dramatically more used than lumbar disc replacements… Cervical discs are easy…What we learned is that it works. I promise you it works. It is an excellent operation, but for a very small, very select group of patients – and I mean very small. In the U.S., it may be viewed as the absolute answer, and that would be a mistake…There is a bigger variation in patients where you can use it (than with lumbar discs) …Initially, I thought it was a motion restoration device. It isn't. I think it is a motion preservation device. It is a load-sharing device. It takes the load off diseased facets and discs. We have seen disc regeneration over time in numerous patients…My personal experience with it is in the younger patients – the 30s guy who is very active and quite debilitated by back pain. That is the ideal candidate for a dynamic system."

CERVITECH'S PCM

The FDA rejected the proposed IDE earlier this year. The company still hopes to get its IDE approved within the next six to eight months. One problem with this product has been migration.

MEDTRONIC

➢ **Bryan.** Enrollment in the key study was completed in September 2004 for this cervical disc replacement with rigid wings, and the company hopes to launch it in the U.S. in 2007. More than 5,500 have been inserted world-wide, and complications so far have included hematoma, incomplete decompressions, etc.

Cervical Discs in Development (*PMA Process*)

Company	Cervical disc	Notes
Abbott/Spinal Concepts	N/A	Has keel and teeth. Clinical trials to start in 2005
Biomet	MinT	Zirconium ceramic. Clinical trials to start in 2005-2006 (little behind Regain)
Biomet/Interpore	Regain	Pure carbon. Expected to start clinical trials in 2005
CerviTech	PCM	FDA rejected IDE in 2004
Johnson & Johnson	N/A	Not in clinical trials yet
LDR	CerviDisc	Ceramic-on-ceramic. Subsidence is an issue. IDE to start in 2005 in U.S.
LDR	Mobi-C	---
Medtronic	Bryan	Titanium with poly core. Approved in Europe. Expected U.S. launch 2007.
Medtronic	Prestige LP2005	Titanium-ceramic composite
Pearsalls	NeoDisc	In human clinical trials
Scient'X	N/A	---
Stryker	CerviCore	IDE expected to be approved in 4Q04
Synthes	ProDisc-C	---
Takiron	N/A	Woven polyethylene fiber matrix with HA coated surface. In animal trials.
Vertebron	N/A	Should be in human trials outside the U.S. in 2005

A Belgian researcher reported on two-year clinical results in Europe with the Bryan disc at one or two levels. He said, "In my own center, we reviewed the first 25 patients at four years, and four of them showed ossification, with two of these remaining mobile. I think NSAIDs may decrease this side effect…We found preservation of motion in 22 of 25, no adjacent degeneration at adjacent levels in 15 of 25. None of the nine who had pre-op degeneration at adjacent levels developed any degeneration at four years."

European Experience with Bryan Cervical Disc

Measurement	Results n=103
Follow-up at 1 year	99%
Follow-up at 2 years	96%
Single level radiologic results out to 2 years	~7 degrees

A Brazilian researcher reported on one-year follow-up of a prospective trial of the Bryan disc.

Brazilian Trial of Bryan Cervical Disc

Measurement	Bryan	Control
1 level	75%	66%
2 levels	17%	30%
3 levels	8%	4%
Surgical time	127 minutes	90.7 minutes
Blood loss	<50 cc	<50 cc
Skin incision size	7 cm	4 cm
Range of motion	- 4.5 degrees	- 8.3 degrees
Complications	No fluid leaks, 1 arterial device migration	2 CSF leaks, 2 device migrations
Fusions	3	1
Post-op kyphosis	2	0
Significant loss of vertebral bone volume	4 cases	0
Heterotopic calcification	3 cases	0

Another study reported that only 11 of 5,500 Bryan discs (0.2%) needed revisions at 4.7 years of follow-up: 4 for infection, 7 for incomplete neural decompensation. There were no mechanical failures, and the explanted devices showed "minimal" surface wear. One of these 11 patients got a new artificial disc, and the others were fused.

One of the issues with the Bryan disc is heterotopic calcification (HO). A U.K. researcher studied HO at one year as well as artificial disc mobility (with single level Bryan discs) at one year in 90 patients to see if there was a correlation. He said, "At one year, 17.8% had signs of HO, and 6.7% had Grade 3 and 4 HO. There was no movement in 10 artificial discs. We found male and older patients were more prone to HO, and Grade 3-4 HO was strongly correlated with loss of movement of the Bryan disc…HO at a severe grade is strongly associated with loss of movement…We use a Cox-2 inhibitor now for all patients…to prevent HO."

➢ **Prestige.** The results of a single surgeon, single level, prospective, randomized IDE study were discussed. Patients in both the Prestige and the control groups showed improvement in all outcomes measured, and the fusion rate for control approached 100%.

12-Month Results of Prestige IDE Study

Measurement	Prestige n=22	Control n=20
Blood loss	22.3	30.5
Average hospital stay	1.1 days	1.1 days
VAS neck pain	Comparable	
SF-36	Identical	
Motion outcome	7.5 degrees flexion/extension	N/A
Segmental lordosis	11 degrees	N/A

SYNTHES' ProDisc-C

Enrollment in the (IDE) clinical trial for this product was completed in October 2004, and the company hopes to launch it in the U.S. in late 2006 or early 2007.

NUCLEUS REPLACEMENT DEVICES

A prosthetic disc nucleus is designed to help patients suffering from degenerative disc disease. They are intended to fill the void in a disc left behind after a discectomy procedure, restoring disc height while permitting normal range of motion.

Nucleus Replacements in Development

Company	Product	Material
Biomet	Regain	Pyrocarbon disc, expected to start clinical trials in 2005
CryoLife	BioDisc	Protein hydrogel
Disc Augmentation Technologies	N/A	Thermopolymer
Disc Dynamics	Dascor	Polyurethane
SpineWave	N/A	Injectable protein hydrogel
Stryker	Aquarella	---
Raymedica	PDN	Pre-formed hydrogen encapsulated in a polyethylene jacket
Replication Medical	Aquacryl, NeuDisc	Dehydrated, compressed hydrogel with Dacron mesh

BIOMET'S Regain. A preclinical baboon study reported good safety and indicated the product is now going into Phase I studies.

DISC DYNAMICS' Dascor. This was described as "like kyphoplasty of the disc." The company claims there are no patent issues because its intellectual property (IP) is on use of the technology in the disc space while Kyphon's is in the vertebra. While that may be debatable, and Kyphon officials

claimed to have IP over the disc space, Kyphon officials indicated they may not make an issue about Dascor, suggesting, "There are ways of working that out."

Dascor was in Phase I trials outside the U.S. at three sites, and that was being expanded to eight sites. In the U.S. the company is doing primate studies.

DYNAMIC STABILIZATION

There was a bit of a buzz at the meeting about dynamic stabilization. Physician comments on these products included:

- "The advantage of the Dynesys system is that you are not compromising the anatomical structures if you get it wrong. The implications are not that big."
- *Brazil:* "I don't think Dynesys is minimally invasive, and I don't think it prevents damage to the muscles…Everyone knows I like minimally invasive, and I don't see a technique as attractive that goes posterior where the disease is anterior. It is like PLIF vs. ALIF."
- *South Africa:* "We went through a significant learning curve with Dynesys, and one thing is absolutely critical with that – screw placement…There is nothing where you need to be more meticulous with screw placement…You can't make numerous passes…I tell patients beforehand that if the screw doesn't seat 100% perfectly, then I will abandon the procedure and do nothing…For me, the advantage is buying time in younger patients."
- *California:* "Dynesys is also attractive from a marketing standpoint. There is great negativity with fusion. We have patients doing great with fusion, but the mentality of people across the country is that fusion is terrible."

Dynamic Stabilization Products in Development

Company	Product	FDA status/ Marketing status
Archus Orthopedics	TFAS	N/A
Medtronic/ Spinal Dynamics	DIAM	Approved in Europe in 2003
Scient'X	Isobar TTL	FDA-approved 2002 / Launched
St. Francis Medical	X-STOP	2004 FDA panel recommended against approval
Zimmer	Dynesys	FDA approved for adjunct use with fusion / Won't launch until PMA complete for dynamic stabilization

MEDTRONIC'S DIAM (Device for Intervertebral Assisted Motion): Medtronic reportedly is trying to get FDA approval to use the 510(k) process, but it may need to do a PMA. A Medtronic official said this device is placed a level above a fusion site to stave off adjacent degeneration, describing it as a kind of "internal traction." He said, "You squeeze it, place it, release it, and it expands. It is held in place by a polycord or tether." A speaker said, "It sort of scares me where you place this device." Other comments about this device included:

- "Interesting concept."
- "It buys you time."
- "DIAM is great for 30-year-olds with a little disc bulge who need a little internal traction."

SCIENT'X'S Isobar TTL: This reportedly has the same indication as Charité and costs about $7,000. Asked how Isobar compares to Dynesys, an official said, "They are the same concept. Dynesys preserved extension, but it can't protect compression."

Scient'X is a French company, with sales revenue for Isobar of about $16 million in Europe, and an expected $10 million in end-user sales in the U.S. this year. It is not clear how well Scient'X can compete in the U.S. market. It has no U.S. sales force, using distributors instead. However, a Scient'X official said, "In Europe, artificial discs did not eliminate the market for dynamic stabilization…Our device can be used with cages or artificial discs, though I don't know anyone doing that. Doctors use this (Isobar) instead of regular pedicle screws… We currently have about 60 U.S. sites…More and more surgeons are concerned with preservation of motion. They are convinced on the technology, and we have to convince them on the product."

Scient'X plans an IDE study in the U.S. and has applied for a PMA. That study is expected to start in 1Q05.

ST. FRANCIS MEDICAL'S X-STOP: A speaker said it was unclear why the FDA advisory panel rejected this device because "the results are pretty impressive." A St. Francis official noted that the panel vote was 5 to 3. He said the panel wanted clinical evidence and the company now has MRIs post-op that should provide that information. In November 2004, the FDA asked for more information, but company officials were optimistic that they could still get approval in 2005.

ZIMMER'S Dynesys: This was the first dynamic stabilization device to be FDA-approved, and it appeared to get the most attention of these devices. A Missouri surgeon said, "Dynesys has more utility. It is minimally-invasive and can be taken out." Another surgeon said, "What's most important about Dynesys is the spacer material. It is more biological, more anatomical than any mechanical device. It can't rupture, degrade, or cause debris. That's why I prefer this. For young patients, this is better than Charité." However, a speaker commented, "It is not really clear what the indications are…but it is the only device to show motion by MRI."

A multicenter, prospective study was reported with 39 consecutive patients with a minimum of one-year follow-up;

87% had open direct decompression as well as Dynesys instrumentation. Researchers reported: 1 intraoperative pedicle fracture, 2 screw loosenings, 1 screw misplacement, 2 explants, 2 decompressions, and 2 extensions.

FUSION PROMOTERS

Key Fusion Promoters

Company	Brand	Product
Chrysalis BioTechnology/ MicroMed Technology	Chrysalin	TP-508
Johnson & Johnson	Healos	---
Medtronic	InFuse	BMP-2
Stryker	OP-1	BMP-7

BMPs are poised to take a double hit – first from artificial discs, and then from CMS reimbursement. Artificial discs are likely to decrease not only use of intervertebral body devices (especially cages) but also BMP. CMS paid an additional new technology fee for BMP, but that has been reduced and will go away in the fall of 2005.

CMS Reimbursement for BMP

Time period	Additional payment
10/1/2003-9/30/2004	$4,550
10/1/2004-9/30/2005	$1,995
10/1/2005 and beyond	0

CMS Criteria for Coverage of BMP

InFuse	OP-1
No posterior code	Only with posterior code (no anterior code)
	No intervertebral body

MEDTRONIC'S InFuse (rhBMP-2) beats JOHNSON & JOHNSON'S Healos

An eight-week rabbit study by Dr. Scott Boden of Emory University compared these two products and found 100% fusion with InFuse and 0% fusion with Healos. The design of Dr. Boden's study mimicked a published, eight-week study by researchers at the University of California, San Francisco (UCSF), in rabbits in 1998 which found that Healos + bone marrow produced good fusions.

One potential criticism of Dr. Boden's comparison is that Healos failed to result in fusion because not enough bone marrow cells were used, but Dr. Boden cited another study which showed a 140% improvement in infusion with marrow harvested from the iliac crest vs. long bones.

8-Week Comparison of InFuse and Healos

Measurement	Infuse n=12	Healos n=12
FDA approval	PMA	510K
Stiffness score	~ 1.5	~ 1.6
Fusion	100%	0
Amount and source of bone marrow cells	---	$9x10^7$ cells from the iliac crest
Relative strength	~ 3.8	~ 1.8
Relative stiffness	~ 2.3	~ 1.2

UCSF Findings with Healos

Measurement	Healos alone	Healos plus bone marrow	Allograft
Fusion	~ 20%	100%	~ 75%
Stiffness score	~ 1.5	~ 1.6	<2
Amount and source of bone marrow cells	$36x10^7$ from long bone	$36x10^7$ from long bone	---

STRYKER'S OP-1 (BMP-7)

A retrospective, single-center study by researchers at the University of Texas, San Antonio, looked at OP-1 for PLIF, reporting successful fusion in 50 of 50 patients by CT at 12+ month follow-up. There was no evidence of excessive bone formation, no stenosis, and no OP-1 related-complications. Bridging bone formed in 100% of patients.

CHRYSALIS BIOTECHNOLOGY/MICROMED TECHNOLOGY'S Chrysalin (TP-508)

This new small peptide – a timed release by product of thrombin placed into allograft – is a promising adjuvant for spinal fusion. A rabbit study found Chrysalin induced bone formation in a dose-dependent fashion. Chrysalin is an osteo-promoter, not osteoinductive.

Preclinical Findings with Chrysalin

Measurement	Allograft alone	Low dose Chrysalin 20 µg	High dose Chrysalin 100 µg
Histology results	No bone formation	Some bone formation	Strong bone formation
Bone formation score	<1	<2	>2
Bone remodeling score	<1	~ 3	~ 4
Fusions by palpation	0	0	36%

VERTEBRAL FRACTURE TREATMENTS

Reimbursement remains an issue, but the AMA's CPT coding committee was scheduled to meet in Miami shortly after NASS, and a new CPT code for kyphoplasty reportedly was on the agenda.

At a discussion group on vertebral augmentation, an FDA official offered some warnings:

- Be cautious about multilevel procedures. She said, "There are a lot of adverse events reported with multiple levels. If you are going to do multiple levels, be extremely careful."
- Calcium phosphate cements are not FDA-approved. She said, "There is less cement used with either vertebroplasty or kyphoplasty, but there are still adverse events... Calcium phosphate cements are not approved, there have been deaths associated with them, and we think they are coagulation-related – based on MDRs."
- Use as little cement as possible. She said, "The maximum amount of cement that should be used in one session (regardless of levels) is <10 cc." Much more cement is used in hips, but the FDA official said that is different because the spine is closer to the aorta, and the anatomy is different.

KYPHON'S KYPHOPLASTY

There appeared to be little to no concern at NASS about the October 2004 ***Spine*** journal article about adjacent segment fractures with kyphoplasty. The general consensus seemed to be that the fractures are real but probably due to normal disease progression. Among the physician comments were:

- *Texas:* "Kyphoplasty is the best procedure you can do…The study (in ***Spine***) is creating a buzz, but it is only one study, and it is not supported by other studies. There is too much other data to the contrary."
- *Florida:* "My kyphoplasty use is about the same as last year, and I expect it to remain stable, but I'm not as enthusiastic as I was. The problem is multiple fractures, not adjacent fractures."
- *Nebraska:* "I'm doing more vertebroplasty now than last year because of cost. I'll do mainly vertebroplasty until there is a better material to inject. Adjacent fractures are not a concern; that's just normal progression."
- *Missouri:* "I'm trained in kyphoplasty, but I don't do it."
- *South Carolina:* "I used to do vertebroplasty, but I stopped when I changed practices, and now I'll start doing kyphoplasty. It is safer and less complicated."

A Cleveland Clinic study tested the stiffness of multilevel treatments in a stress model. A researcher reported, "Contrary to what has been believed previously, kyphoplasty does not significantly increase adjacent level strains." He added:

- Augmentation by kyphoplasty does not significantly alter multilevel segment stiffness.
- Higher adjacent level strains occur at subsequent fractures than at index.
- Adjacent level strain is distributed on both the superior and inferior adjacent vertebrae.

A Stanford study looked at the behavior of kyphoplasty vs. vertebroplasty under repetitive loading conditions (100,000 cycles). A researcher said, "Fractured vertebrae treated with vertebroplasty didn't significantly change under repetitive loading conditions, but kyphoplasty did. Kyphoplasty was more likely to show progressive loss of height…and to show a progressive collapse of cancellous bone."

Another researcher reported that a retrospective study of a cohort of 222 consecutive patients with vertebral compression fractures found the risk of subsequent fracture increases with the number of fractures. Sixty percent of additional fractures were seen directly adjacent to kyphoplasty, and 40% were done at non-adjacent levels.

Kyphon has long claimed that kyphoplasty restores height better than vertebroplasty, and a study by Dr. Joseph Lane of the Hospital for Special Surgery agreed with that. He found balloon kyphoplasty enhanced height reduction >5 fold over vertebroplasty with positioning, noting, "If height restoration is the goal, kyphoplasty is clearly superior."

COMPETITORS

Other than vertebroplasty, competitors to Kyphon were pretty quiet at this meeting, and they did not appear to be getting much attention.

ARTHROCARE. An official pointed out that the company's Parallax system has been revised and doctors have the choice of using their RF wand or a Kyphon balloon. He also commented that their cement has tantalum markers in it to help track the flow.

SPINEOLOGY'S OptiMesh. OptiMesh has a C.E. Mark, and an official estimated that about 40 surgeons in the U.S. currently are using OptiMesh for vertebral fractures. OptiMesh is just that – a mesh (polypropylene) bag that is placed in a vertebral cavity and then filled with granules of bone chips with a cannula. The official said the company still needs a PMA for interbody fusion use of the device. That trial is ongoing, with 200-300 patients being enrolled who will have two-year follow-up.

REIMBURSEMENT

The medicolegal environment is likely to get worse, an attorney warned. He predicted it could have serious implications for spine surgeons:

- Increasing tension between manufacturers and physicians, with manufacturers feeling pressured by trial lawyers to take a more active role in training physicians. He said, "There are some certification programs now, but I think there will be a lot more given by manufacturers, and that will put pressure on physicians to take the training because if the physician doesn't do that and something goes wrong, the first thing the plaintiff's lawyer will say is, 'You should have taken the training that the manufacturer offered.'" Doctors also may blame manufacturers for not training them properly if something goes wrong.
- Informed consent (also called informed choice or shared decision-making) will be more important.
- Direct-to-consumer advertising will increase, and courts have held that this puts more responsibility on manufacturers to inform patients about risks. He said, "I think that will translate into manufacturers telling physicians very specifically what they have to tell patients about the devices." Advanced technologies already are being introduced to make this easier for manufacturers and physicians.
- Implied warranties are areas where patients will try to get at physicians.
- Consumer fraud claims may increase. Plaintiffs may allege there is something you didn't tell them – especially with new devices which may or may not have extensive testing and research.
- Courts will put more burden on manufacturers to be more careful in marketing. He cited the lawsuits against firearm manufacturers, suggesting orthopedic device companies could see similar lawsuits, claiming they were negligent in how they marketed their products.

MISCELLANEOUS

ABBOTT LABORATORIES: Abbott has a growing presence in spine. First, it bought **Spinal Concepts**, and then during NASS 2004, it bought **Spine Next**. Sources agreed that Abbott should be watched and is starting to build "critical mass" in spine – in fusion and non-fusion – but they did not think Abbott would try to buy Kyphon. A source said, "Abbott is systematically and aggressively moving into fusion and non-fusion. They are acquiring what they need to be a real player in this field."

What does Spine Next bring to Abbott? A source cited Wallis, a next-generation, posterior dynamic stabilization system similar in concept to Dynesys. He said, "The only difference is there are no screws with Wallis…You never need to tighten it, and there has been no loosening in thousands of patients…Doctors will recommend trying this before Charité…It is a very easy, very quick solution…It's only about a 10-15 minute procedure." A U.S. IDE is supposed to start in 1Q05. It is expected to be marketed to early stage disease in younger patients.

Abbott has a lumbar disc, Inspire, that is expected to start U.S. clinical trials in 2005, and it has a cervical disc in preclinical development. A source said, "So, Abbott doesn't need to acquire artificial disc technology, but it could need a nucleus replacement."

A source said Abbott wants to have a comparable presence in both cardiology and orthopedics.

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