Trends-in-Medicine

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by Lynne Peterson

SUMMARY

Interest by patients and spine surgeons in artificial discs is extremely high. Usage is expected to take off dramatically when the first disc is approved, and this is attracting a plethora of companies to this space. Even Boston Scientific and Guidant reportedly are looking at entering this market. ♦ Spine surgeons continue to favor kyphoplasty over vertebroplasty, but growth in kyphoplasty procedures is expected to slow due to cost, reimbursement, rumors CMS will issue a CPT code, and improving results with vertebroplasty. Kyphoplasty is good medicine, but it's bad from a business sense. ♦ 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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Medicare reimbursement is increasingly an issue for spine surgeons. In a recent survey, more than half of the spine surgeons questioned said they have limited their Medicare participation, and 7% have stopped participating altogether. However, spine surgeons are very interested in new technology, including artificial discs, vertebral augmentation (kyphoplasty and vertebroplasty, BMP, and bone graft extenders.

ARTIFICIAL DISCS

This was the hot topic at NASS. Doctors are very, very interested in these. Most sources intend to get trained as soon as possible, with some even planning to get trained out of the country ahead of approval to be ready when artificial discs get the nod from the FDA. A surgeon said, "I would train right away and use right away. And I might train outside the U.S." A Midwest doctor said, "Everyone will get trained the minute one is approved. The first year will be crazy." A California doctor said, "The first to be approved will be very intriguing." A Nevada doctor said, "I'm very excited about them, and I would get trained if the training were available. I've already observed some. And I won't wait to start using them after I'm trained (and they are approved)." Another surgeon said, "There will be a race between artificial discs and new biologics for growing a new disc. Then, eventually, we all hope the biologics work. I think the uptake of artificial discs will be quick."

Yet, some doctors who plan to get trained do not expect to start using artificial discs immediately. A Texas doctor said, "I'll train right away, but I'll wait a year to use them. If something is effective at one year, it probably has a benefit." A Vermont doctor said, "I'll get trained when they are approved, but I won't use them for years." A New York doctor said, "I'd get trained and then wait and see for six months."

Radiologists as well as spine surgeons are likely to use artificial discs. A California doctor predicted, "The real growth will be in the (interventional) radiologists."

Most sources agreed that it is not technically difficult to put in these discs, particularly if the surgeon is already doing anterior fusions. There will be a need for some – but not much – special instrumentation, and the cost of this is not expected to be a barrier to use. Durability also is not an issue with any of these devices, sources said. A Mississippi doctor said, "Only surgeons who do the

anterior approach to fusion will do artificial discs at first." A Massachusetts doctor said, "It is not technically difficult if you know how to do anterior fusion, but you need training." A California surgeon said, "I will train in the anterior approach (in anticipation of artificial discs), but an access surgeon will be there, so minimal training is needed." Another surgeon said, "I've seen some failures by investigators, so it does take some expertise."

Artificial discs solve many problems: They (a) allow better sagital balance than fusion which increases stress above and below the fused site, (b) avoid graft harvest, and (c) are expected to be less expensive than BMP. A Pennsylvania doctor said, "TDRs allow better sagital balance; fusion increases stress above and below. TDRs also avoid graft harvest and are less expensive than BMP."

Patients are already asking about artificial discs, and they are expected to be very accepting of these as TDRs (total disc replacements). Patients have come to accept total knee replacements (TKRs) and total hip replacements (THRs), and doctors said they think of TDRs and similar procedures. In this environment, doctors reported pent-up patient demand, and they predicted uptake would be very fast. A Mississippi doctor said, "I think uptake will be quick. The issue will be over-use not slow uptake."

A poster by researchers at the Hospital for Special Surgery in New York found that the contraindications to TDRs mean that TDRs will not eliminate the need for fusions surgery. They concluded, "Predictions that TDR will replace fusion are premature…It is more likely that growth in TDR implantation will result from changes in surgical indications, so that patients who are treated non-surgically today might be treated surgically in the future."

Measurement	Fusion patients n=56	Non-fusion surgery patients n=44	Total
Contraindications to TDR	100%	89%	95%
Average number of contraindications	3.25	1.3	2.45
Contraindications			
Lumbar stenosis	96%	36%	---
Facet arthrosis	66%	27%	---
HN with radiculopathy	20%	55%	---
Spondylolisthesis	77%	2%	---
Spondolysis	13%	0	---
Scoliosis	21%	0	---
Osteoporosis	18%	0	---
Post-surgical deficiency of posterior elements	20%	7%	---
Pseudoarthrosis	2%	0	---

The three discs closest to market are:

➢ **JOHNSON & JOHNSON'S SB Charité.** This will probably be the first artificial disc on the market (in late 2004 or early 2005). A 60-patient study found that the key to good results is patient selection. The procedure too an average of 1.5 hours.

Measurement	SB Charité	Control (BAK Cage)
Change in Oswestry Score	-20.1 50.0 pre 25.0 post p<.001	-17.2 45.9 pre 23.5 post p<.001
Change in VAS	-29.4 73.5 pre 30.4 post p<.001	-23.2 68.2 pre 34.0 post p-value N/A

➢ **MEDTRONIC'S Prestige**. The pivotal trial is expected to finish enrollment in December 2003, with two-year follow-up from the last patient. A Medtronic official said equivalency to fusion should be enough for FDA approval, and then the company will seek to show an advantage over fusion. It is expected to be on the market in 2006. The advantages cited for Prestige over ProDisc or SB Charité are: long (10 year) clinical history in Europe, stainless steel composition, and good biomechanics.

➢ **SYNTHES' ProDisc.** Doctors are most excited about this right now. It reportedly is about a year behind Prestige. A six-month study of 53 patients randomized to either ProDisc or no surgery found that ProDisc offered greater motion at L4-L5 ($p<.05$), but L5-S1 was difficult to assess (a trend but not statistically significant). At six months, motion at the untreated L3-L4 was not significantly better for either group. A surgeon said, "ProDisc has the most promise, but all the artificial discs are far from what they need to be." An investigator said the operating time averages 75.4 minutes. Another surgeon said, "ProDisc is easier than SB Charité, but the results are the same. Metal-on-metal is the way to go."

Although doctors are excited about these discs, they admitted they are not perfect. The big question about TDRs is what to do if a patient needs a revision. Few spine surgeons believe that the first artificial discs will last a lifetime (>40 years), and no one really knows how to get them out. The current plan appears to be to fuse the site if the TDR fails, but that is not an ideal situation. This makes it problematic to use TDRs in younger patients (<age 50), which is exactly the patients who need them the most. A surgeon said, "The problems for the future will be: revisions, making them more forgiving so the average Joe can do it, and creating modular discs." Another source said, "I don't think there will be a way to revise artificial discs."

The ideal disc was described as one that:

- Is semi-constrained to restore stability to the disc space.
- Restores height, motion and spatial balance.
- Protects the adjacent space.
- Permits future fusion.
- Can stand the test of time (>40 years).

A multitude of competitors are working on artificial discs. Sources said the key companies to watch – after J&J, Synthes, and Medtronic – are:

- **BIOMET** and **STRYKER**. Both of these companies have more experience with range of motion (from hips and knees) and motion preservation than Synthes or Medtronic. J&J's artificial disc people reportedly are working with their hip/knee experts in Poland to take advantage of their experience.

- **BOSTON SCIENTIFIC** and **GUIDANT**. Boston Scientific reportedly has made a decision to become a player in spine and had a five-person "SWAT" team at NASS to scope out the space (perhaps to buy an artificial disc company). Guidant also is looking at getting into spine, perhaps through artificial discs, and has been sounding out some key opinion leaders.

Artificial Discs in Development

Company	Nucleus	Total lumbar disc	Partial lumbar disc	Total cervical disc
Biomet	---	---	AISS	---
CerviTech	---	---	---	PC
CryoLife	BioDisc	---	---	---
Disc Augmentation Technologies	Thermo-polymer	---	---	---
Interpore	---	---	---	Titanium/ ceramic disc
Johnson & Johnson/Link	---	SB Charité	---	---
Medtronic/Spinal Dynamics	---	Maverick	---	Bryan and Prestige
Raymedica/Medtronic	---	---	PDN-Solo and Solo-Excel	---
SpineCore	---	FlexiCore	---	CerviCore
SpineWave	Injectable disc nucleus	---	---	---
Stryker	Aquarella	---	---	---
Synthes/Surgical Dynamics	---	ProDisc	---	ProDisc
Zimmer	---	---	Spiral	---

Comments by sources on various discs:

- **Interpore's** disc. This ceramic dome on a titanium keel appears to be far away in a very crowded field, and the company was very vague in discussing it.
- **Medtronic's Maverick.** The pivotal trial is still enrolling patients, with about one third currently enrolled. It is not expected to be on the market until 2006. A Nevada doctor said, "Maverick is the most promising. It is metal-on-metal and has a good center of rotation."
- **SpineCore's FlexiCore.** A trial started in the U.S. in September 2003. A New England doctor aid, "I don't like the design. It is radically different and too constrained."
- **SpineWave's nucleus.** This is thought to still be in pre-clinical testing.
- **Cervitech's PC.** A pivotal trial is due to start in January 2004. A source estimated it would take 18 months to enroll patients, with two-year follow-up required on the last patient. Thus, this is not expected on the U.S. market until 2008. It uses the same materials as the SB Charité. It reportedly is totally non-constrained and has a calcium/ phosphorus coating to encourage bone ingrowth.

Beyond artificial discs

There will be a race between artificial discs and biologics for growing a new disc, a source said. He commented, "Eventually, we all hope the biologics work."

VERTEBRAL AUGMENTATION: Kyphoplasty vs. Vertebroplasty

An estimated 700,000 vertebral compression fractures (VCFs) occur in the U.S. annually, generally in osteoporotic patients. That's one every 45 seconds. An expert estimated that one-third of these become chronically painful, with the other two-thirds going undetected and pain-free, and a patient who has one VCF has a 1.92% rate of further fractures. Whether the VCF if detected or undetected, the patient does not spontaneously regain lost height. A speaker commented, "Kyphosis begets kyphosis."

Open surgical repair for VCFs has a poor outcome, so doctors have turned to other options:

1. Medical management.
2. Vertebroplasty, which has become the preferred procedure for interventional radiologists.
3. Kyphoplasty, which has become the preferred procedure for spine surgeons.

Who is the perfect patient for vertebroplasty or kyphoplasty? One expert said, "The perfect patient is someone who has been sleeping for three to four weeks in a recliner….You can feel a cleft with no risk of leakage…In those patients, the pain is gone essentially immediately. I wouldn't do these procedures

in patients with pain that has lasted more than a year. In the absence of mobility, it is hard to help people after a year; the fracture becomes fixed, and I have trouble getting those patients better." Another surgeon said, "One of my things in the workup is palpating the spine…My criteria is pain related to local tenderness." A third said, "You don't want to do these procedures in patients with chronic pain, fixed position, or where you can't define where the pain is coming from."

Spine surgeons generally prefer Kyphon's kyphoplasty to vertebroplasty, and Kyphon has introduced new balloons and tools. A poster also discussed doing single-balloon kyphoplasty, suggesting this could reduce operating time and be useful for chronic VCFs. A Tennessee doctor said, "The instrumentation is simple and easy to use."

However, enthusiasm for kyphoplasty is waning somewhat, and vertebroplasty is gaining few converts among spine doctors, who are starting to see less advantage to kyphoplasty over vertebroplasty. The dangers of vertebroplasty are declining with experience, the height restoration is less than previously thought with kyphoplasty, and kyphoplasty is considerably more expensive. In addition, kyphoplasty is being linked to additional adjacent fractures, and it is not a profitable procedure for spine surgeons to perform.

Doctors estimated that over the next year, their kyphoplasty procedures will continue to grow slightly, but that growth is starting to slow. Doctors doing the procedure are not anxious for their volume to grow because of the low reimbursement. A California doctor said, "I was going to advertise kyphoplasty, but I didn't because of the reimbursement. I do it because patients do so well; they do amazingly well. I think spine surgeons are pretty much maxed out on kyphoplasty." A New Mexico surgeon said, "I'm doing about three a week now, and in six months I'll be doing 2-4 a week. That is the max I want to do. If I wanted to do kyphoplasty solely, I could do 10-12 a week, but at $500 each, that's all I want to do." A Texas doctor said, "Referrals are getting better, but I don't advertise because I don't want to do just kyphoplasty." A Tennessee doctor said, "There is a slow increase as people hear about it and request it. I've not been trying to grow referrals."

Furthermore, none of the spine surgeons questioned who are not doing kyphoplasty now plan to start. A Nevada doctor said, "In my town, our radiologists do vertebroplasty. They didn't like the balloon pressure of kyphoplasty. None of the spine surgeons in town do kyphoplasty, and none of them plan to start. The general practitioners in town are all aware of these procedures, and they refer to the radiologists." A Wisconsin spine surgeon said, "I'm not convinced of the value of kyphoplasty in most patients, so I will remain on the sidelines. If I did anything, it would be vertebroplasty unless I couldn't get height restoration with positioning, which you usually can do." A West Coast doctor said, "I can't afford to do it. It is not cost effective at $700, but I think it is a great procedure." An Oregon doctor said, "If I start, it will be something less expensive than kyphoplasty. Kyphoplasty has a nice product, but the hospital reimbursement is too low. Our hospital allows it, but discourages it." A Texas spine surgeon said, "Our radiologists used to do mostly kyphoplasty and are moving to vertebroplasty. The orthopedic surgeons do kyphoplasty, and I may start vertebroplasty."

A Kyphon official claimed the company has trained 2,600 doctors, including ~2,450 spine surgeons, but very few interventional radiologists. The company also has started a pilot program with primary care doctors, using 15 sales reps and doing local co-op marketing with Merck.

Among the issues affecting attitudes toward kyphoplasty and vertebroplasty are:

Pain relief. Both vertebroplasty and kyphoplasty are effective at relieving pain. Doctors repeatedly commented that the results can be quite dramatic with both procedures. A speaker said, "Pain reduction with kyphoplasty and vertebroplasty are comparable." Another speaker said, "There is a good body of literature supporting the effectiveness of vertebroplasty for pain relief. In French studies, there was 80% pain relief in osteoporotic patients and 50% relief in tumor patients." A California doctor said, "Kyphoplasty and vertebroplasty are both pain relieving procedures, not deformity correction procedures." A Texas doctor said, "The pain reduction is similar."

A 46-patient study of quality of life after vertebroplasty found that all five health-related quality of life measure improved by two weeks and remained improved out through six months. Pain decreased immediately and remained improved. Vertebral height restoration was associated with better quality of life scores two-weeks post-procedure.

Cement leakage. The concern with cement leakage is embolization to the lungs, where the cement can harden, arrhythmia and hypotension. Cement leakage is less a problem with kyphoplasty (generally <10% of cases) than with vertebroplasty because a thicker cement is used with kyphoplasty, and this used to be perceived as a major advantage for kyphoplasty over vertebroplasty. A Kyphon official said 37 MDRs had been filed with the FDA about side effects with kyphoplasty, and this includes ~33 reports of extravasations, out of 35,000 procedures to date.

However, with experience, cement leakage is occurring less frequently with both procedures. A speaker said, "In (some vertebroplasty) studies, there were cement leaks in 30%-70% of patients….(but) in another study the cement leakage rate was 7.7%, so there is a trend to more experienced individuals controlling where the cement is going." Another speaker said, "Three years ago, leakage was less than 10%, and not that I've done a lot of cases, it is not even an issue." A Tennessee

doctor said, "I've had some leakage periodically (with kyphoplasty), but the patients haven't been symptomatic."
A new kyphoplasty technique was discussed that can further reduce the chance of cement leakage. With this cavity containment technique, the surgeon inflates the balloon, removes it, puts in a little cement, and re-inflates with a balloon, creating a "shell." Then, the rest of the cement is inserted. A speaker said, "I only occasionally do a cement shell…It sounds good and looks great in pictures, but it isn't needed very frequently." Another surgeon said, "I use this technique in 10%-15% of cases -- a lot in myeloma cases where patients have holes in the bone and I want a backstop."

Height restoration. There is little to no height restoration with vertebroplasty, and data is building that height restoration is obtained with kyphoplasty in only a select group of patients – those who are treated early (within two months) of the fracture occurrence. This was estimated at 10%-20% of patients. Some vertebroplasty advocates also claimed that much of the kyphoplasty height restoration is due to patient positioning before the procedure. An Illinois doctor said, "The issue is that in a percentage of cases, particularly older, healed fractures, the balloon is unable to reduce the deformity because the fracture healed or partially healed." A Vermont doctor said, "Height restoration is better with vertebroplasty. Kyphoplasty is taking a good procedure and making it more expensive. The benefits (of kyphoplasty) are all theoretical." A California doctor said, "Height restoration is not clinically significant with either kyphoplasty or vertebroplasty."

Timing. Medicare requires that doctors wait four to six weeks after diagnosis of a VCF before it will reimburse for either vertebroplasty or kyphoplasty – because some fractures heal (stop hurting) on their own within that timeframe. Thus, many patients are treated too late to achieve height restoration.

Reimbursement. Kyphoplasty is not a profitable procedure for spine surgeons. It is good medicine, but reimbursement is not good (varying from $500 in some states to a high of $1400 in at least one, but generally in the $700-$800 range). One surgeon said that, on average, he does 1.6 kyphoplasties per patient. Spine surgeons repeatedly pointed out that most other procedures they do are better revenue generators, so doctors said they do **not** plan to encourage referrals or advertise to expand their patient base.

Kyphoplasty could become even less profitable if Medicare reimbursement is lowered. There currently is no CPT code for either kyphoplasty or vertebroplasty, but all Medicare carriers are reimbursing for both. There are reports that a CPT code may be published in January 2004 to go into effect in 2005 that would set kyphoplasty reimbursement at ~$590 (plus any biopsy fee, etc.) vs. ~$510 for vertebroplasty. For many doctors this would be a reduction in reimbursement. A speaker said, "Companies cannot request a CPT code, only the medical societies can do that. NASS and other societies are waiting for a little more peer-reviewed data before submitting to get a code."

Kyphon officials claimed no CPT code is on the near horizon, but several other sources insisted a code is under consideration, and the rate being discussed was ~$515 for vertebroplasty and ~$595 for kyphoplasty. In either case, there is likely to be a code eventually, and there is little doubt that the reimbursement will not be favorable for kyphoplasty, though it shouldn't be terribly negative either. A speaker said, "As surgeons, none of us will ever be happy with reimbursement. Remember the carriers' mission in life is to not pay. We go through that (reimbursement hassles) on a daily basis…I have a packet of articles that are in print, and a letter and I send those along with before and after information on the patient, and most of the time that works and we get reimbursed, but it takes work on our part."

Sources do not expect any reduction in hospital reimbursement (DRG payment) in the near future. They explained that kyphoplasty patients, unlike vertebroplasty patients, generally spend one night in the hospital. Under the current DRG, they said hospitals generally make a little money on kyphoplasty when one level is done, break even on two levels and lose money on three or more levels. Doctors said their hospitals are not discouraging the procedure where it is established.

There were reports that doctors in Boston and Seattle are being investigated by the Office of the Inspector General (OIG) for Medicare fraud for billing kyphoplasty as osteotomy. This could not be confirmed, but speakers did discourage doctors from billing kyphoplasty this way.

Lack of new doctors starting kyphoplasty. None of the spine surgeons questioned who currently are not doing kyphoplasty plan to start doing it. These doctors said they refer to interventional radiologists and are satisfied with that system.

Additional fractures. It appears that there is a small but real increase in adjacent – but not remote – fractures following either vertebroplasty or kyphoplasty, but these fractures can be treated with another procedure and generally do not lead to further fractures. This is not discouraging doctors from doing either procedure, but it also is not causing doctors to shift from vertebroplasty to kyphoplasty. A surgeon said, "I don't buy the idea that putting in cement predisposes a patient to future fractures. I think you actually prevent future fractures…I feel comfortable saying when we're doing kyphoplasty, we are not predisposing patients to adjacent and remote fractures."

A chart review of 42 consecutive kyphoplasty patients from September 2001 to July 2002 found 17 patients had subsequent fractures. The fractures occurred at every level.

There was no statistically significant difference based on gender, age, BMI, number of index fractures, history of tobacco use, cancer, NSAID use or steroid use – but the numbers for these subgroups were small. Twenty-one percent of patients experienced a subsequent fracture at adjacent levels over the first two months, but adjacent fractures were significantly less likely to occur after that.

Growth of vertebroplasty by interventional radiologists. Interventional radiologists, who perform vertebroplasty as an outpatient procedure, are doing more and more of vertebroplasty, and sources expect that trend to continue. Sources said it is unlikely that many interventional radiologists will switch to kyphoplasty (NOTE: though Cleveland Clinic radiologists did switch), and one reason cited was that interventional radiologists usually do not have hospital admitting procedures for overnight stays. Apparently, interventional radiologists find the vertebroplasty reimbursement sufficient to encourage growth of that procedure. Thus, more growth is expected in vertebroplasty than kyphoplasty, which may further encourage spine surgeons to refer patients to interventional radiologists.

Number of levels that can be done. One expert said he would limit kyphoplasty to two levels at one session unless a patient was going to receive a total of five, then he would do three at one session and two at another session. Another surgeon said, "I wouldn't do three or four at a time, either."

No usage guidelines. The American Academy of Orthopedic Surgery has not issued guidelines for vertebral augmentation. A speaker said, "They are afraid of the liability…There are liability issues…There are plenty of smart lawyers who can make something dramatic out of it."

Lack of long-term data on kyphoplasty. There is long term data (>10 years) on vertebroplasty, but not on kyphoplasty, but most surgeons did not consider this a major issue. Two-year data from a 155-patient prospective kyphoplasty study, with 100 patients followed out to two years. Mean height restoration was 40%. Patient satisfaction was maintained from day 7 to 24 months. Pain was reduced >50% at all follow-up time points.

Timeframe	Days pain interfered with activity	VAS pain score	Patients unable to bend	Patients unable to lift 10 pounds	Patients unable to stand
7 days	---	~8.8	25.0%	50.0%	40.1%
30 days	10 days/month	~8.4	4.5%	24.6%	18.7%
90 days	10 days/month	~8.1	3.1%	18.3%	14.5%
12 months	~2.5 days/month	~7.9	3.7%	22.2%	14.8%
24 months	~2.5 days/month	~7.8	3.0%	16.0%	18.0%

Non-U.S. sales. European doctors are not expected to do much kyphoplasty because of the cost.

Competitors. There are new competitors on the market and additional competitors in development, but overcoming the Kyphon patent – which a Kyphon official said covers "any balloon in bone and creation of a void in bone by any means" – is proving difficult, and spine surgeons are not very excited about any of these.

- **Synthes'** hinged curette. A speaker said, "This is the easiest to deal with…It basically is a tool for making a cavity."

- **Interpore's AOM**. This is a procedure somewhat like kyphoplasty without a balloon. There is a curette for making a void in the bone, and then a cannula (instead of a needle) is used to insert a toothpaste-like cement. An Interpore official said most sales so far have been to doctors who weren't doing either kyphoplasty or vertebroplasty.

Doctors expressed little interest in AOM. It is likely to find a few users, but sources did not think it was a threat to either vertebroplasty or Kyphon's kyphoplasty. One of AOM's problems is likely to be what doctors described as Interpore's inability to market well. The cost is about one-third of kyphoplasty, but it is still more than vertebroplasty. It is aimed at spine surgeons, not interventional radiologists. A surgeon said, "Why buy this when you can just use the kyphoplasty kit without the balloon. You don't have to buy the balloon, though the company won't suggest that." A California doctor called AOM a "cannula injector system," adding, "The advantage is you can use thicker cement, but if you are good at vertebroplasty, you can do it with a needle. Only select spine surgeons will be interested in this. The experienced guys who realize a balloon is not always necessary may find AOM attractive, because Kyphon won't market non-balloon use of their system."

- **Medtronic.** An official indicated Medtronic has a product in the idea stage; it hasn't entered animal trials yet.

- **Jupiter Surgical.** Reportedly, this company has a "better" cannula for doing vertebroplasty, so that thicker cement can be used.

- **Johnson & Johnson.** J&J is testing something in Europe.

- **Parallax,** which was recently bought by **Arthrocare.** A source said there is a lag in stopping the flow of cement with this vertebroplasty device. An official said, "We are seeing more spine surgeons doing our vertebroplasty. Mostly they are moving from doing just kyphoplasty to doing both kyphoplasty and vertebroplasty."

  Arthrocare also has a new system, the Cavity Spine Wand, that can be used to treat VCF. This system uses RF to make a cavity

in the bone. The initial focus in on spinal tumor patients. The cost is $1,200 per wand, with one wand needed per patient. The Cavity Spine Wand uses a smaller introducer cannula than Interpore. There is no CPT code yet for this, but an official said doctors may be able to get paid under the partial corpectomy code. Arthrocare is attempting to get a C-code for vertebroplasty, and is hopeful this can be resolved quickly. An official said, "Rita Medical filed for a CPT code for tumors a year ago…We are trying to sell our system to CMS as a way to reduce the tumor complication rate."

➢ **Spineology's OptiMesh.** The idea sounds good: a polypropylene bag to hold avoid leakage, but it isn't cement or DBM that is put in the bag. Rather, it is MTF (granules of bone chips) or another filler. A cavity is created using a drill, then the mesh is introduced through a cannula, and then the mesh bag is filled with a biologic granular material (MTF). A company official claimed the advantages are: elimination of cement and only one incision.

Spineology has a CE Mark, and three different mesh sizes are sold in Europe:

- 1500S for interbody fusion with pore size 1.
- 1500E for VCF with pore size 1.
- 500E for VCF, with pore size 2 (smaller than pore size 1) to restrict the flow of other fluid materials (like BMP). This product has differential porosity (80% size 2 and 20% size 1). The larger pore size is designed to encourage flow in the posterior part.

Doctors who looked at OptiMesh were dubious about it. A surgeon said, "I'm very skeptical. If OptiMesh works the way the company says, it would be competitive, but I'd need to see it work as elegantly as the balloon (kyphoplasty) does…If it doesn't allow leakage at all, it could be bad because there could be no interdigitation of the cement, and I think that supports the bone. Will the bone heal, and will it get rid of the pain?" Another source said, "It is a device looking for an indication. I don't know how the company will be able to justify the additional cost." A Virginia doctor said, "Packing loose bone hard enough is an issue. And does it have structural stability? I don't see how it would interdigitate." A California doctor said, "I can't make up my mind about this." Another West Coast doctor said, "OptiMesh is kind of odd. It needs more documentation before people will use it."

PROCEDURAL SAFETY FOR PHYSICIANS

A 12-month study of physician exposure to ionizing radiation from fluoroscopy during vertebroplasty had some surprising results (that also apply to kyphoplasty). In fact, some doctors said this data, of all the data presented at the meeting, was the most likely to change what they did when they went home. The study found that radiation exposure was well above federal occupational limits until new shielding protocols were instituted. A researcher said, "Without shields, my annual occupational dose limit would be exceeded with 34 procedures per year. With reduction measures and shields, I could do 6,700 annually without exceeding federal limits…The (shielding) techniques added less than a minute of time to overall procedures."

In particular, the gloves physicians use to shield their hands not only aren't sufficiently protective, but they can increase the amount of danger radiation received. The speaker said, "Gloves don't help; they hurt. They essentially trap the low/medium level radiation in your hands…And you ***must*** have glasses."

BONE MORPHOGENIC PROTEINS

A million bone graft procedures are currently done annually, and 50% of these are related to spine fusion. Two BMPS currently have FDA approval – Medtronic's InFuse (BMP-7) and Stryker's OP-1 (BMP-2) – but only InFuse is approved for spinal fusion. There also are other BMPs in development. A BMP expert said, "It is not clear to me which is the best BMP…The most osteoinductive are BMP-2, BMP-6 and BMP-9. BMP-7 is osteoinductive, but not to the same level as the others…So, relative potency may vary."

Some of the enthusiasm for BMP has waned. Doctors generally believe it improves fusion in anterior fusions with a cage, and patients like it much better than a bone graft. In fact, the key reason cited for using BMP was avoiding the harvest of iliac crest bone. A doctor said, "I think the patient needs to be involved in the decision, and when I present the data to the patients, most choose BMP…Only one patient in the last 18 months wanted a bone graft, and now she wishes she had never done that."

Doctors are trying to find ways to use BMP less frequently, mostly because of cost. A speaker said, "We agree that BMP works in anterior fusions, but I don't know that it would be fair to say that about off-label use…The purpose of these devices (BMP) is to heal bone…and the job of the surgeon is to pick the right patient and the tools to achieve that goal…Other than lack of crest harvest, I'm not sure I want BMP to take credit for overall good outcomes (with spinal fusion surgery)."

Some doctors also are trying to use less BMP when they do use it. The current, approved dose of InFuse is 20 mg per side. An expert said, "Could you get away with 15 mg? I don't know…I don't think you can get away with 10 mg."

Experts also were advising against off-label use of BMPs, particularly in posterior fusions, and the message appears to have been heard. Few sources currently are using InFuse off-label. Dr. Scott Boden of Emory University, a recognized BMP expert, said, "There are now enough patients who've had InFuse in the LT cage, and the fusion rate is >99% -- the same

as in the pivotal and pilot trials. That is a reliable number and impressive. But all bets are off for off-label use. I don't think we know what happens with other things in the same cage. I think BMP can compensate for a bad cage, but with a good cage, you may not need that…I would not advise using the collagen sponge 'as is' out of the kit...It doesn't work in monkeys, and there have been inconsistent results in a Japanese study. Some people are trying to bulk up the sponge...and we presented ways to augment the sponge by mixing ceramic chips or allograft chips. That is now in clinical trials in humans, but there are no results yet…I haven't tried to use InFuse without iliac crest in posterior fusion…In another six to nine months, it will be clear (whether this works) but for now it is unclear what the consistency of response will be using it that way."

Currently, Medtronic's InFuse (BMP-7) owns this space, and sales are likely to continue strong for another year. Yet, doctors reported that InFuse is not helping Medtronic sell them other Medtronic products, except the LT cage. They also said that their use of InFuse is not hurting any other companies, just other Medtronic products.

Questions discussed about BMP and InFuse included:

- ***Does BMP work in smokers?*** An expert said, "Most studies say smoking interferes with fusion…Cox-2s probably interfere, too, but the evidence is less clear, and whether there is the same or less interference is not clear...but I stay away from any NSAIDs….It is unclear if you need a higher dose of BMP in smokers or if the usual dose works…Time will tell."
- ***Should BMP be used in revision surgeries?*** An expert warned, "When you are up against scarring, against inch thick gristle, I don't know how BMP will work…Be careful using any BMPs off-label…We can wait another year or two (for trial results)."
- ***Does BMP cause over-exuberant bone?*** An expert said, "I've done thousands of animal surgeries and not had it be an issue…The only example is if there is a huge hematoma in an open space that dissects."
- ***Can BMP be used with bone expanders (ceramics, etc)?*** An expert said, "I don't think anyone knows the right answer…Most of these products are not regulated like BMPs…The vast majority of bone extenders are unsubstantiated…even in animal data.

The cloud on the BMP horizon is the artificial disc. At one audience discussion session, no one thought the advent of disc replacements would put them out of business. However, about 25% of the doctors said they will only do artificial discs when they are available, another 25% predicted artificial discs would cut fusions or use of BMP substitutes by more than 50%, and the rest said artificial discs would cut fusion and BMP use substantially.

Is BMP having an impact on use of electrical stimulation [e.g., Smith & Nephew/Oratec's IDET(intradiscal electrothermal annuloplasty)], a minimally invasive outpatient procedure for chronic low back pain caused by herniated disc? There was a paper at the NASS meeting suggesting that electrical stimulation increases production of BMP, but an expert said, "If you have an adequate dose of BMP and 99% fusion, then electrical stimulation can't make it better…If there is an inadequate dose of BMP, electrical stimulation could potentially enhance fusion…If you use a DBM which has BMP activity but maybe not as much as BMP does, and you augment that with electrical stimulation, then, in theory, you could bring that up to BMP level, but that that is just theory." An Arizona doctor said, "I haven't seen any impact on electrical stimulation from BMP."

Other BMPs

- **rhBMP-6.** Rat and rabbit studies look promising.

- **Johnson & Johnson/DePuy/Orquest's Healos (rhBMP-14, MP52).** The carrier for this BMP is Healos, an osteoconductive mineralized collagen matrix. It is provided as lyophilized strips. There have been good results in animal models, and a speaker said the radiographic healing rate was 58.3% compared to 25% with autograft at six months in non-human primates.

- **Stryker's OP-1 (BMP-2).** At this meeting, there appeared to be little excitement about or interest in OP-1, a bovine collagen matrix of either granules or putty. OP-1 has a humanitarian device exemption (HDE) from the FDA to treat long bone fractures (trauma) that fail to heal in a normal time; it is still in clinical trials for spinal fusion. A study of single level fusion in degenerative spondylolisthesis showed no systemic toxicity, no ectopic bone formation, and no product-related complications. Fusion was 94%, and a researcher explained why he thinks it wasn't higher, "It is a biologic and…This is the most challenging model – a non-instrumented fusion. There is greater instability in this model… (and) the host biology is an issue because the average age was in the upper 60s, the patients were mostly women, and the sample size was small…Based on these results we believe OP-1 is safe and likely as effective, if not more effective, than autograft in this model."

Measurement	Autograft n=12	3.5 mg OP-1 putty n=24	Historical rate with autograft
Radiographic fusion	40%	65%	45%
≥20% Oswestry improvement	60%	94%	---

A 402-patient study of OP-1 with the Medtronic LT cage found OP-1 was associated with a statistically significant difference in many surgical endpoints, less blood loss, a shorter surgical time, a higher fusion rate, an improved Oswestry disability score, higher PCS scores, and an earlier return to work.

BONE GRAFT EXTENDERS AND OTHER PRODUCTS

Interesting comments on these products included:

- "If I would make one plea, it would be: If we buy it, then people will sell it. We need to stop buying things before we know they work. We need to pressure industry for a higher burden of proof."
- "There are a lot of things that work well in adolescent that don't translate to older adults…so pediatrics is unique and definitely an area where we can use bone graft extenders."

Demineralized Bone Matrix (DBM)

The FDA mandates that each DBM lot be obtained from a single human donor. However, a speaker said there still is considerable inter- and intra-variability of the BMPs in commercially-available DBM, "We are not really sure what we are getting. There are currently 20 different commercially-available DBMs…It would be nice for companies to do an Elisa (assay) and say, 'In this product we have this profile of BMP'…or say the standard is this…I still use DBMs but really as a bone graft extender. I don't think we can consider them stand-alone products. These are not substitutes for BMP." Another expert said, "The only DBM I know that has been tested in humans is Osteotech's Grafton, and it did not work as a stand-alone product...so what I think is the most potent DBM does not stand alone…but that doesn't mean it couldn't be used in a cage."

Factors that contribute to the variability in DBMs include:

- Demineralization time
- Acid application
- Temp
- Defatting agents
- Sterilization process (especially)
- Carrier
- Storage

Platelet gels and concentrates

There was little enthusiasm for **platelet concentrates and gels.** A doctor said, "I tried them and stopped. I was not convinced they made a difference at all…and in looking for literature support, I can't find it." Another expert said, "There are two papers (at NASS) of interest on platelet gel from one manufacturer which are not terribly encouraging…One is in interbody fusions where there was a lower fusion rate with platelet gel, and the other failed to show a benefit. And paper in **Spine** last month also suggested – in an uninstrumented single surgeon series -- that there was a decrease in fusion from 90% to 61% with platelet gels…Theoretically, the reason for lower fusion rate with platelet gels is an inhibitory effect on BMP, but that has not been proven…There are differences between platelet gels…and, much like growth factors and DBMs, you need to take each on its own and not assume all work the same." Another doctor said, "We are doing a randomized, prospective trial comparing 25 control autograft patients with 1-2 level surgery to 25 patients with AGF and cancellous chips in a mesh cage. We have 18 month follow-up at this point, and the CT scans show no difference in fusion rate (with platelet gels), but we are not seeing deleterious effect either." A third surgeon said the data on these products are conflicting and predicted they will be a topic of controversy for the next year or two." A fourth doctor said, "Platelet gel inhibits bony fusion, but patients feel they heal faster, and the wound closes faster."

MISCELLANEOUS

Motion technology

Dynamic stabilization is becoming a buzzword. Medtronic's DIAM, Zimmer's Dynesys, and St. Francis Medical Technologies. If these are successful, sources said they likely would be used earlier in the care of back patients, but would not reduce fusions.

Companies worth watching

- **NuVasive**, a privately held company working on minimally invasive spine technology.
- **St. Francis Medical Technologies**.

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