Orthobiologics: The Evolving Frontier
Ethical Coding: How is it Possible? Cash Only?

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AOSSM 2015
Disclosure

- The following relationships exits:
  1. Royalties and stock options—none
  2. Consulting income—none
  3. Research and education support—Funding SIMR research support
  4. Other support

- No conflict related to this talk
New Technology

- Life blood of improving medical care
- Always involves some risk
- Still needed in 2015
- Widely understood that FDA regulates this
- Not widely understood that this regulation is patchy
FDA

- Closely regulates—most drugs—require FDA approval
- Regulates many orthobiologics
  - Stem cells regulated
  - Others (PRP) slide in under 510K approval
  - Still others used “off label” (rotator cuff patches)
- Use of orthobiologics in investigational products not approved by FDA limited to IRB approved and registered human clinical trials (HCT)
PRP

- Approved by FDA via 510K process
- FDA’s 21 CFR1271 allows PRP “not to follow traditional regulatory pathway” Beitzel et al.
- Nearly all cleared for use with bone grafts
- Use of PRP otherwise is “off label”
- Activated PRP may not be legal
Off Label Use

- Allows use of previously cleared products for used not approved or cleared by the FDA
- 85% of BMP used off label
- 30% of medications used off label with little support (AAOS Now 2014)
- Concerns
  - No premarket review for adverse events
  - “can lead to unsupervised experimentation”
  - Serious problems developed with off label use of BMP
- To check status:
  - Biologics Products Establishments (http://www.fda.gov/-BloodVaccines/ucm121134.htm)
Why not use off-label??

Medtronic Infuse Bone Graft
The Medtronic Infuse Bone Graft has been linked to life-threatening complications in patients who were given Medtronic off-label. Medtronic bone graft complications include swelling of the airways, which can cause difficulty breathing, speaking and swallowing. Medtronic Infuse has also been linked to retrograde ejaculation which can lead to male sterility. A number of Medtronic lawsuits allege the manufacturer illegally promoted the Medtronic bone product for off-label uses.
Gene therapy

- Cell and Gene Therapy (CGT) trials closely regulated by FDA (http://www.fda.gov/BiologicsBloodVaccines/guidanceComplianceRegulatoryInformation)

- “extensive manipulation of human blood, bone marrow or other sources, for the purpose of obtaining enriched stem cell populations, renders them a somatic cell therapy product subject to licensure by the FDA"
Stem Cells

- These can pose substantial risk
  - Fatal late onset leukemia in stem cell trial
  - Brain and spinal cord tumors in intrathecal allogeneic stem cell transfers
- Involves “considerable clinical safety issues”
Stem Cells

- Cole “current clinical use is outstripping the evidence to support their use” Orthop Today 2014
- Orthop Today 2014 FDA approval is not needed “when stem cells are harvested, manipulated, and reimplanted in the same patient that same day”
- Not exactly…
“Can Stem Cell Therapy Replace Surgery?”

In many cases, yes. However, a full evaluation is needed first to determine if your condition is a good fit for stem cell therapy.

“Can Stem Cell Therapy help Back Injuries, Rotator Cuff and Hip Injuries, and offer an Alternative for Knee Replacements? Yes”
FDA

- With the exception of Carticel, ALL orthopedic stem cell applications investigational
- IND (investigational New Device) application required
- Often actual treatment performed overseas
- FDA identified use
  - Warning letter
  - Court action via Department of Justice
Actual FDA Statement

- “FDA Warns About Stem Cell Claims” (www.fda.gov/For Consumers)
- Hemacord only stem cell product approved by FDA
- All others “a clinical investigation that has been submitted to and allowed to proceed by FDA”
“Relaxed Oversight”

- Single, same day procedure
- “minimal manipulation” only
- What’s “minimal manipulation”? 
  - FDA draft guidance pending 2015
  - Material must stay onsite due to infection risk
- Stem cell clinic successfully prosecuted in 2014 and closed
- Clearly, “manipulated” cells illegal
- If the cells are not manipulated, are they really stem cells?
“If you are considering stem cell treatment in the U.S., ask your physician if the necessary FDA approval has been obtained or if you will be part of an FDA-regulated clinical study. This also applies if the stem cells are your own. Even if the cells are yours, there are safety risks, including risks introduced when the cells are manipulated after removal”
Basic Science

- Adipose-Derived Stem-Cell Treatment of Skeletal Muscle Injury

- Not effective
• Adult Human Mesenchymal Stem Cells Delivered via Intra-Articular Injection to the Knee Following Partial Medial Meniscectomy. A Randomized, Double-Blind, Controlled Study

  • More meniscus “volume”
History lesson

- 1990’s Blue Shield decides all shoulder arthroscopy “investigational”
- Refuses to pay
- Times have changed
  - Level one studies-not really
  - Level four data-probably
  - Widely established treatment option now
  - Patient demand for minimally invasive surgery-most likely
AAOS CPG lesson

- Very little high-quality level one data for most of what the first world does
- Doesn’t mean it doesn’t work
- “clinical equipoise” popularized by Pedowitz makes level one studies difficult
Ethical coding

- What’s legal?
- What’s supported by guidelines?
- Does it have a code?
- What’s ethical?
  - How established is the procedure?
  - Chance of benefit?
  - Chance of risk?
Medicare

- Must use CMS accepted codes
- Medicare will not pay otherwise
- $10,000 line item fine for incorrect coding
- Illegal to be medicare provider and charge cash
- Illegal to bill medicare for products used in research protocols
Workers’ compensation-varies state by state

- Treatment not preauthorized not paid for
- “honor system” allows billing and subsequent denials without criminal penalty
- Can bill patient’s insurance for denied treatment
- Workers’ compensation patients may not be balance-billed
Private insurance

- Health insurance plans with confirmed non-coverage policies on PRP and PRP related therapies:
  - AETNA
  - BLUE CROSS BLUE SHIELD
  - CIGNA HEALTH PLANS
  - HEALTH NET
  - OXFORD HEALTH PLANS
  - UNITED HEALTHCARE

- [http://www.hss.edu/PRP_Cover_Letter_Stationary.pdf](http://www.hss.edu/PRP_Cover_Letter_Stationary.pdf)
Easy Decision-Steroid injection

- Level one data-plus/minus
- Widely established treatment option
- Has a code
- Can’t bill office visit with injection code if not supported
- Benefit-good short term
  - ?long term
- Risk-minimal
  - Infection
  - Steroid flare
Moderate Decision-PRP injection

- Level one data-most against
  - Surgical-poor
  - Outpatient-marginal
- Not widely established
- Has a code-experimental
- Benefits
  - Perhaps some short term
  - No long term
- Risk
  - Infection-trended in Burke’s study
  - Stiffness, neoplasia to date not an issue
Codes

- Category III (investigational) code 0232T
  - Insurance won’t pay
- Per AAOS “all work associated with this procedure in the office is inclusive to 0232T”
  - Imaging
  - Injection
  - Associated office work
  - Blood draw
Bill cash?

- Only option for reimbursement
- Legal? Not in Medicare or Workers’ comp
- Ethical?
  - Informed consent is key
  - Some discussion of benefit
  - Some discussion of lack of established benefit
  - Some discussion of risk
- “The patient read about it in the sports section and wanted it” is not adequate
Difficult decision - Stem Cells

- Level one data - minimal
- Established procedure - no
- FDA approval - required
- Benefit
  - Unclear
- Risk
  - Infection
  - Neoplasia - perhaps significant
  - Unknown risks - potentially significant
- Quick web search offers numerous offers for “stem cell therapy”
Manufacturers’ disclaimer significant

- Biomet MarrowStim Concentration Kit:
  - “the safety and effectiveness of this device for *in vivo* indications for use has not been established”
    http://www.biomet.com/regions/northAmerica/canada.cfm?passedCategory=osteobiologics

- Harvest BMAC product:
  - “Warning: The safety and effectiveness of BMAC for *in vivo* indications has not been established.”
    http://www.harvesttech.com/harvest-bmac-product-details
Bill Cash?

- Clearly Illegal for allogenic products
- Define “minimal manipulation”??
- Use of FDA regulated products outside of IRB approved research protocol violates human subjects act
- Grounds for criminal charges
Most difficult - Ozone treatment

- Investigated as an option in early 1900’s
- Level one data - zero
- Established procedure - no
- Code - no
- FDA approval - no
  - Only legal in 11 States
- Benefit??
- Risk?
  - Invasive procedure for no proven benefit a real problem
Bill Cash

- Only option
- Not legal Medicare, Workers’ compensation or 39 states
- Ethics of billing an invasive procedure with little if any substantial benefit—questionable
Summary

- Orthobiologics an evolving arena
- Not much level one evidence for most of what we do
- Billing probably should be limited, use limited to established study protocols
- Cash pay in some arenas legal
- Never ethical without appropriate, unbiased informed consent
References

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