Rehab Protocols and Best Practices in Orthobiologics

BOSTON SPORTS & BIOLOGICS

NHMI FALL SYMPOSIUM

I HAVE NO RELEVANT FINANCIAL RELATIONSHIPS TO DISCLOSE

I WILL NOT DISCUSS OFF LABEL USE OR INVESTIGATIONAL USE IN MY PRESENTATION

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LEARNING OBJECTIVES

- Explain how to tailor rehabilitation programs based on the type and location of orthobiologic therapy administered
- Evaluate the current evidence on timing and progression of rehabilitation after orthobiologic procedures
- Understand the treatment goals and healing cascade as it relates to post procedure activity and rehab progressions

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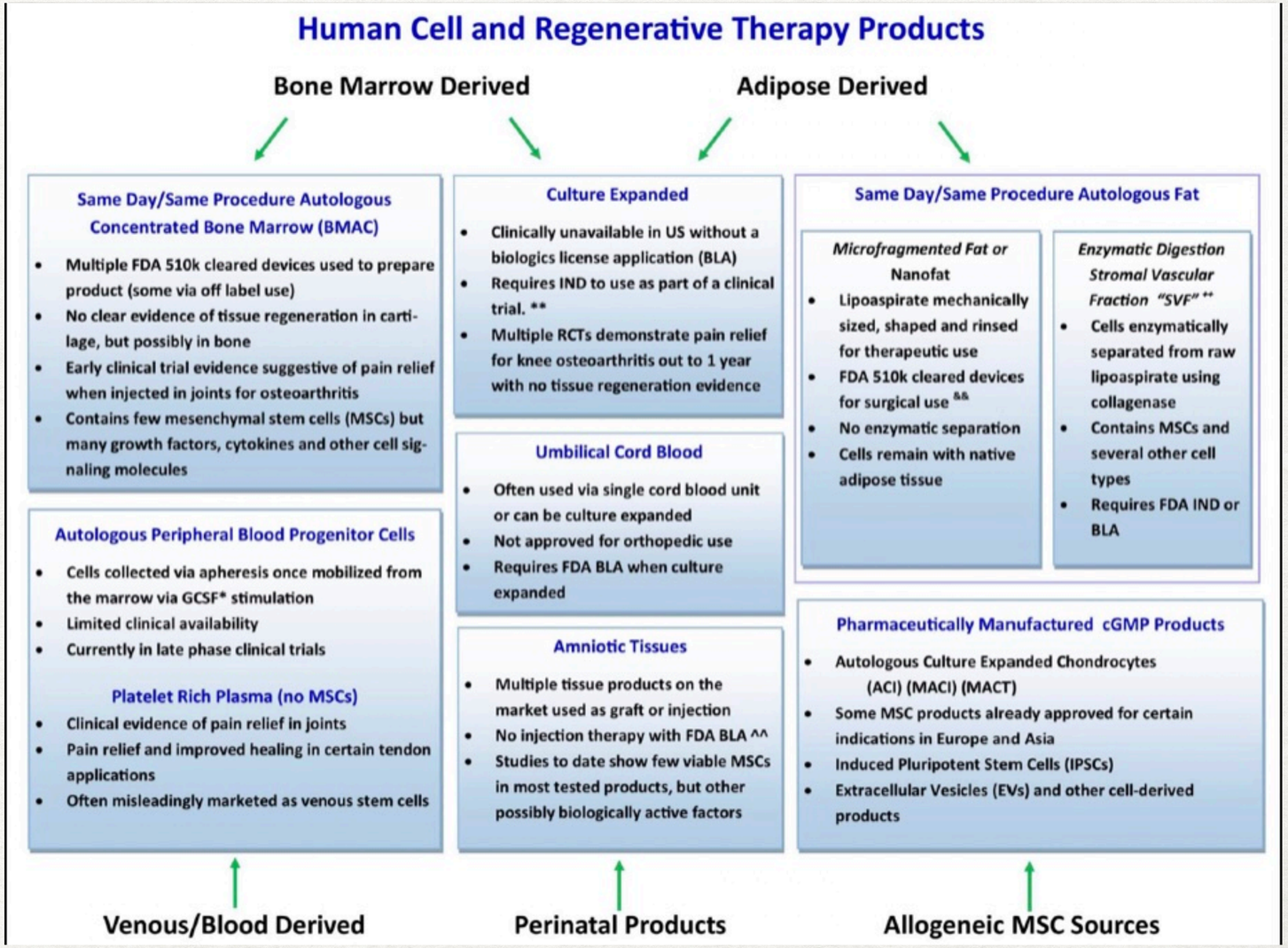
DEFINING ORTHOBIOLOGICS

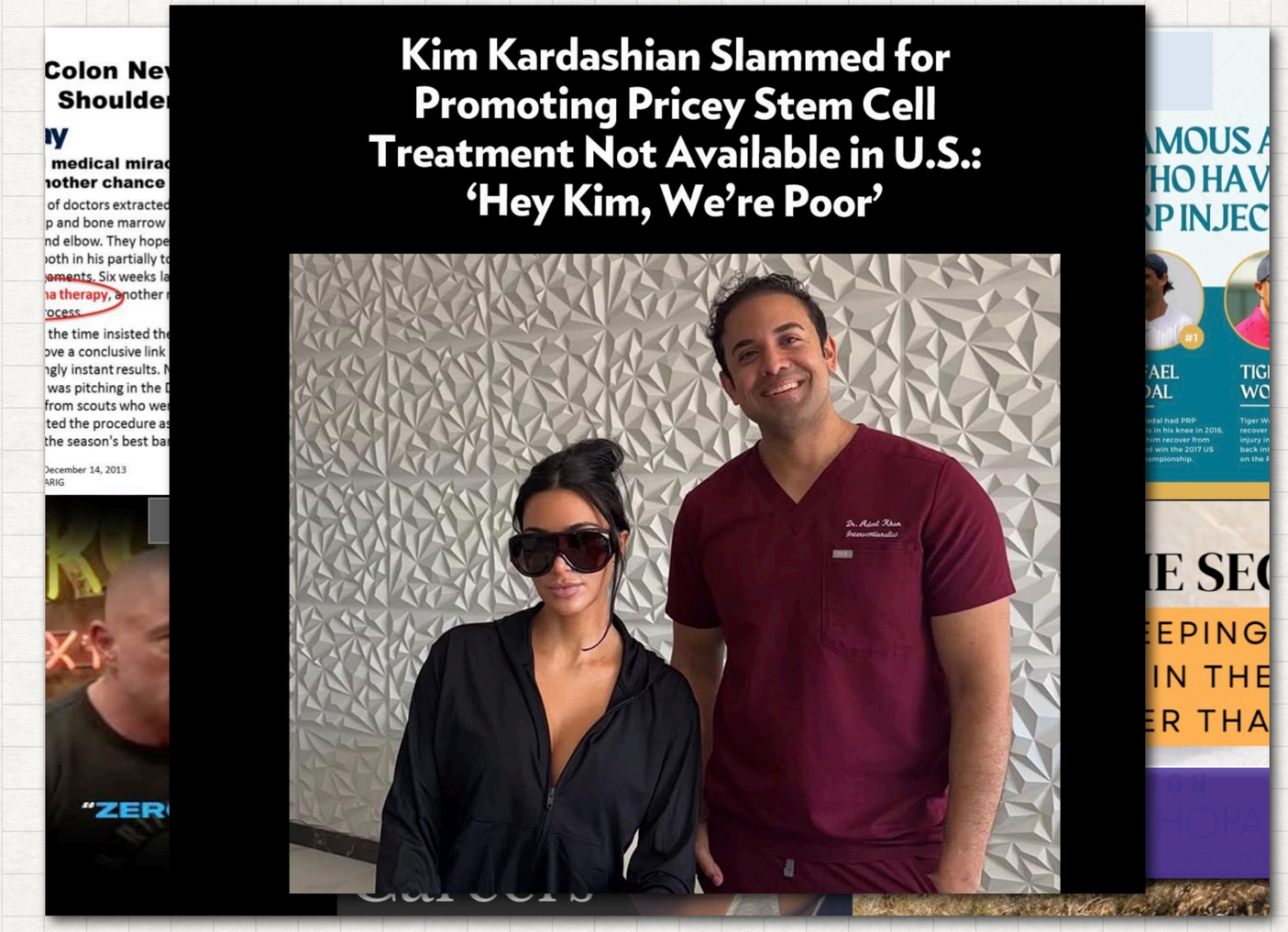
- Biological products, often sourced from the patients own blood, fat, or bone marrow, that are used to stimulate and accelerate the body's natural healing processes for muscles, bones, joints, and other musculoskeletal issues



DEFINING ORTHOBIOLOGICS

WHAT'S LEGAL

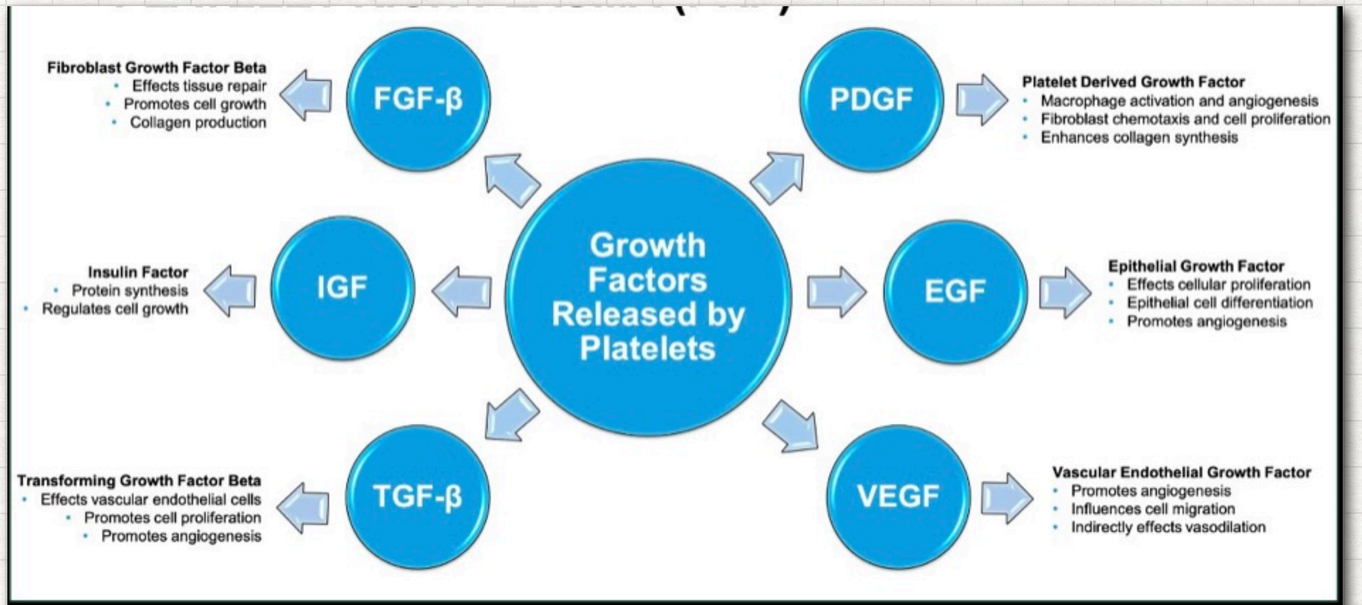
- Section 361 HCT/Ps
- Homologous use
- Minimally manipulated
- Not combined with a drug
- Autologous use
- Does not have a systemic effect

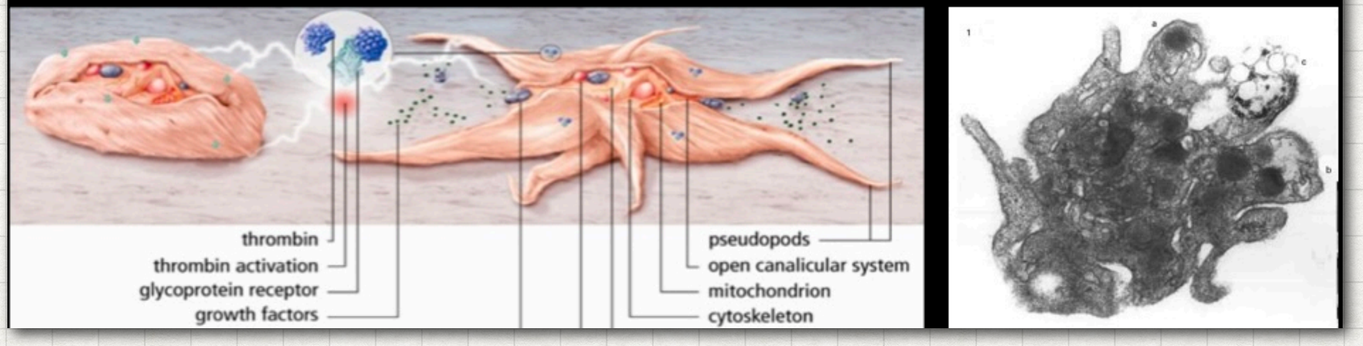


WHAT IS PRP

HEMATOLOGY REVIEW

- FDA definition is an autologous blood product with a higher concentration of platelets than baseline values
- Platelets- small, anucleate, discoid blood cells synthesized in the red bone marrow. Once synthesized, platelets are released into the peripheral circulation
- PRP contains a cocktail of cytokines and growth factors to promote/ restart the healing cascade

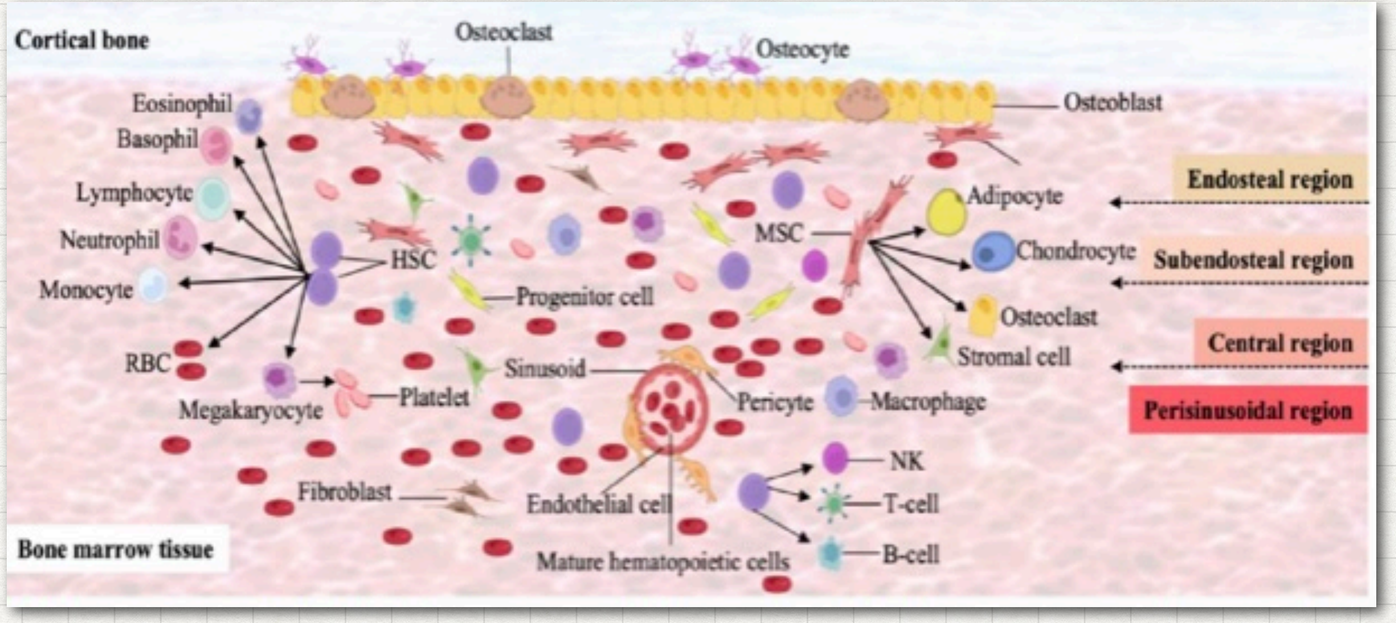


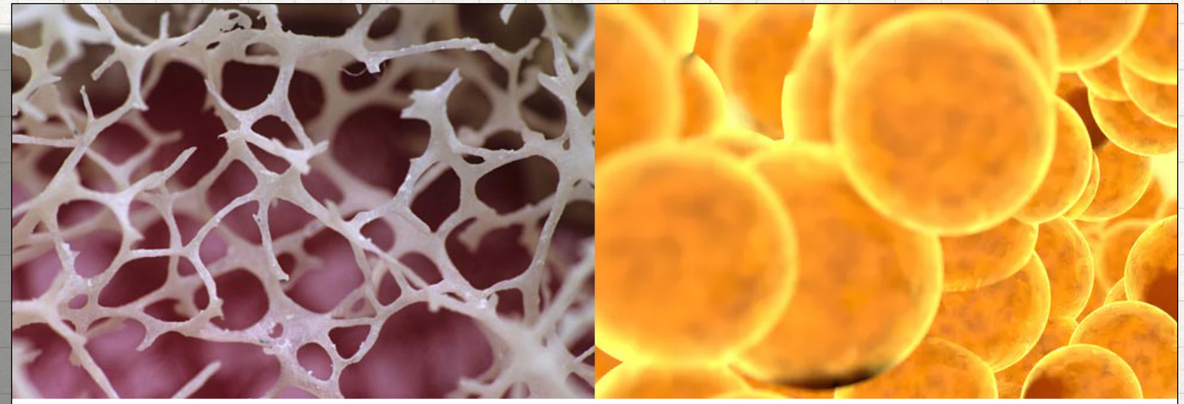


WHAT IS A "STEM CELL"

BMAC/MFAT

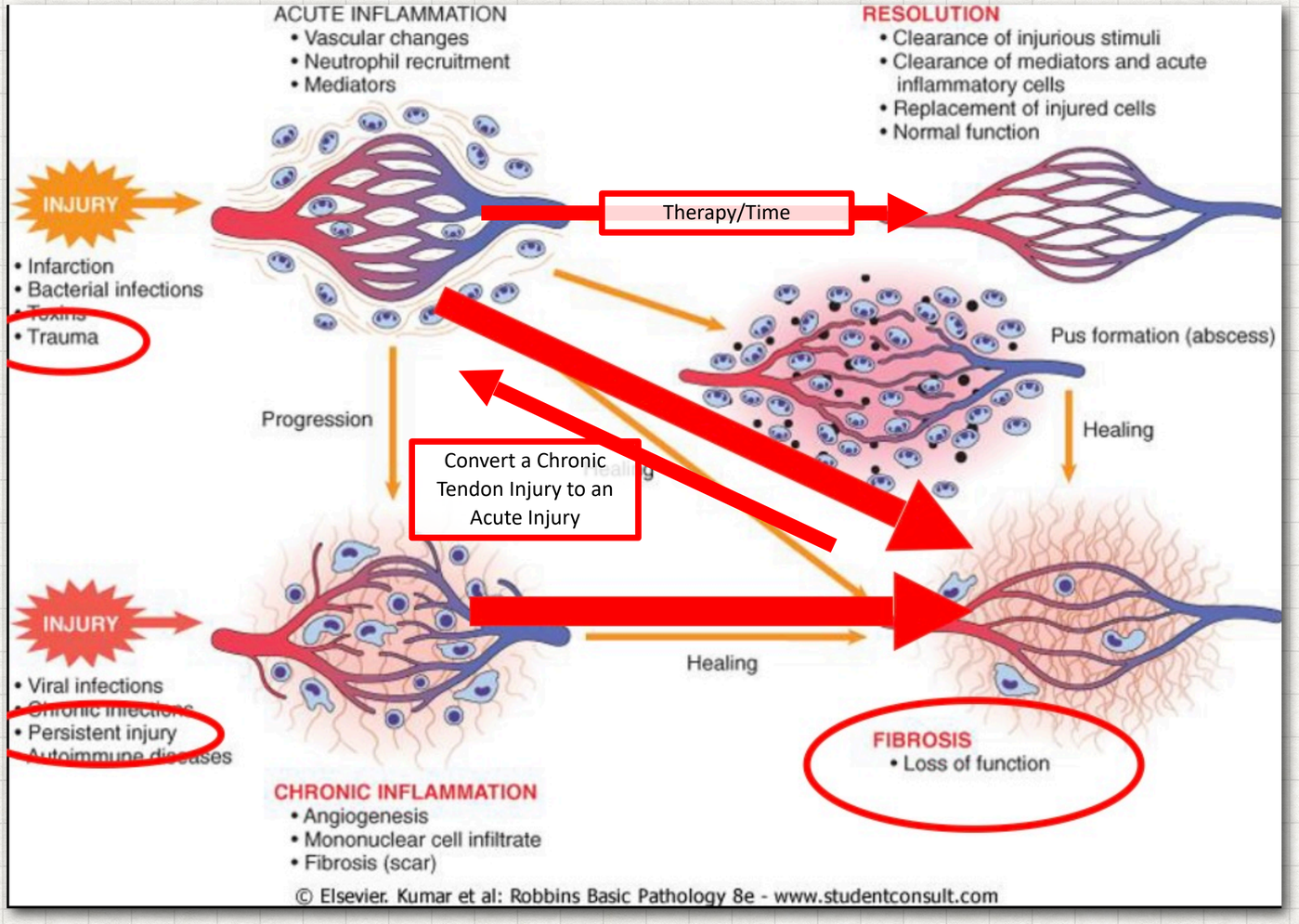
- Stem Cells are a cellular population with the ability to self-replicate through mitosis to form daughter cell lines
- Typically classified based upon their tissue of origin
- BMAC is composed of concentrated MSCs that are responsible for cell signaling, (Neo)angiogenesis, improve cell recruitment
- MFAT provides 3D scaffold





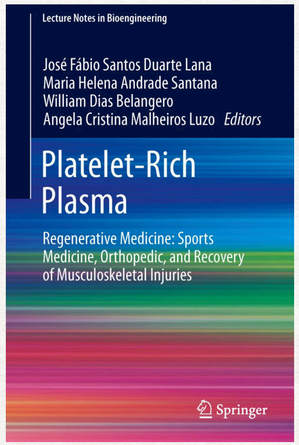
WHAT IS THE GOAL

CHRONIC TENDINOPATHY



PHASES OF TENDON HEALING

RATIONALE BEHIND LOADING



Inflammatory Phase

Proliferative Phase

Remodeling Phase

Phases of Tendon Healing

The three principal phases of tendon healing, although they are not sharply delineated, are: (a) the inflammatory phase, (b) the repair phase, and (c) the remodeling phase (Fig. 17.1). The rehabilitation program should progress

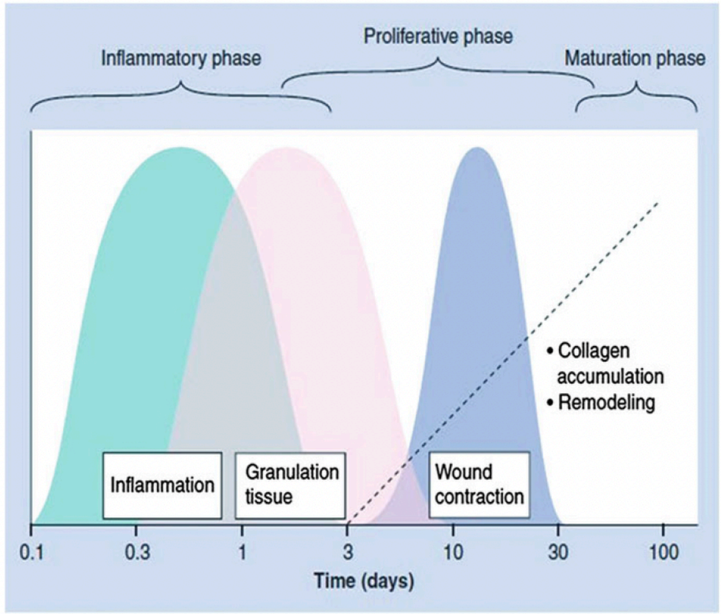
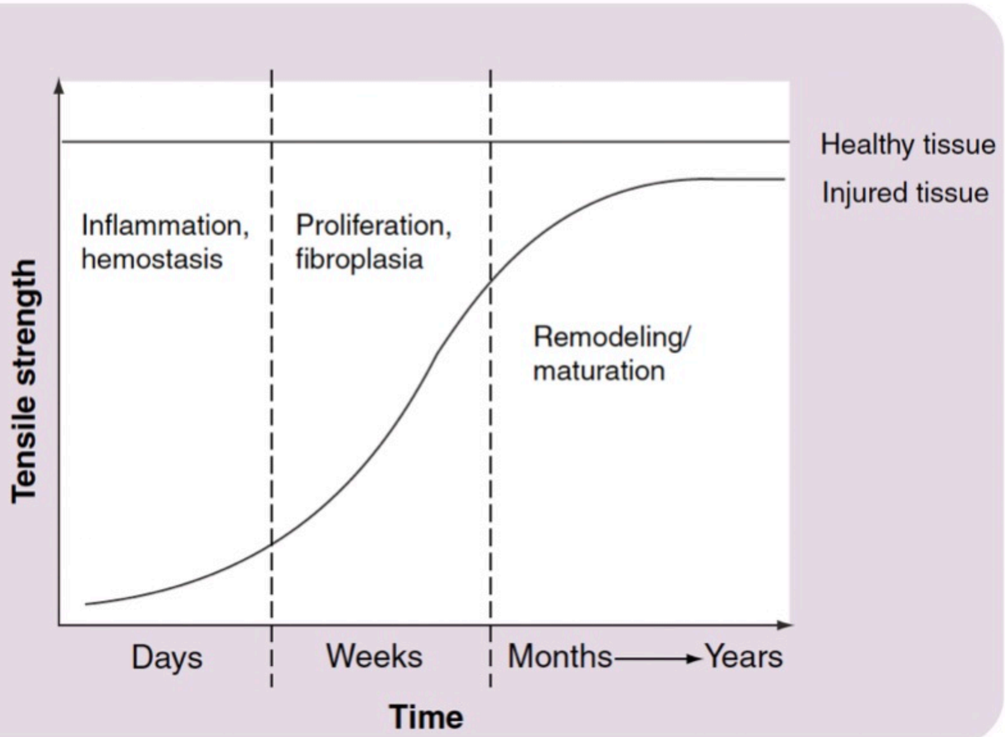


Fig. 17.1 The phases of tendon healing. Adapted from Mautner et al. (2011) and Kumar et al. (2004). Used with permission of Future Medicine and Elsevier, respectively

Figure 3. Healing phases during tendon regeneration as suggested by Gomez and colleagues.



The various stages are discussed in the text. Data from [27].

IMMOBILIZATION FOLLOWING PRP

WIEGERINCK ET AL (2014)

- Injected 10 cadaveric lower limbs with 5 ml PRP colored with blue dye using a peppering technique under ultrasound guidance into the achilles tendon
- Injected into 3 separate portions of the tendon 1.5 cm apart
  - 5 specimens were manipulated through 100 cycles of ankle dorsiflexion and plantar flexion to simulate walking
  - 5 specimens were allowed to rest in a prone position for 15 minutes
- No significant difference in the two groups of dye/PRP spread

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Comparison of Postinjection Protocols After Intratendinous Achilles Platelet-Rich Plasma Injections: A Cadaveric Study

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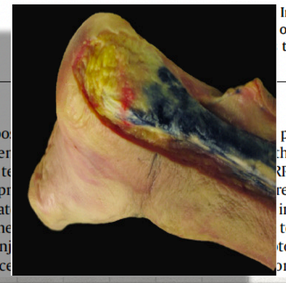
ARTICLE INFO

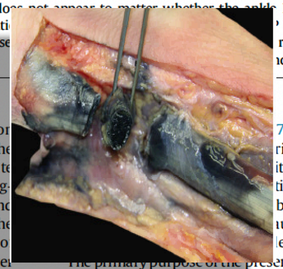
Level of Clinical Evidence: 5

Keywords:
Achilles tendon
India blue dye
platelet-rich plasma (PRP)
tendinitis
tendinopathy

ABSTRACT

The purpose of the present investigation was to evaluate the distribution of intratendinous injected platelet-rich plasma (PRP) after 15 minutes of prone resting versus immediate manipulation simulating weightbearing. Ten cadaveric lower limbs were injected under ultrasound guidance with PRP dyed with India blue ink. The dyed PRP was injected into the mid-portion of the Achilles tendon, after which 5 specimens were placed in the prone position for 15 minutes (simulating rest) and the remaining 5 specimens were manipulated through 100 cycles of ankle dorsiflexion and plantarflexion (simulating walking). Thereafter, the specimens were dissected, and the distribution of the India blue dye was ascertained. In the simulated rest group, every specimen showed dyed PRP in the Achilles tendon and in the space between the paratenon and tendon. The median craniocaudal spread of the PRP was 140 (range 125 to 190) mm. In 4 of the simulated rest tendons (80%), the distribution of PRP extended across the entire transverse plane width of the tendon. In the simulated motion group, every specimen showed dyed PRP extending across the entire transverse plane width of the tendon and in the space between the paratenon and tendon. The median craniocaudal spread was 135 (range 115 to 117) mm. No statistically significant difference was found in the amount of craniocaudal spread between the simulated motion and rest
In conclusion, it does not appear to matter whether the ankle has been moved through its range of
or maintained stati injection into the mid-portion of the
tendon. The precise realm remains to be discerned.





The po plasma (PRP) or 7–12). One postinjection protocol
Achilles ter the platelets on the ring. In contrast, others (7) have
damaged te RP at the lesion site ition for at least 10 to 15 minutes
(1–5). A pr reaches the desig tial weightbearing for the first few
nated anat injection into and been recommended (8–10). These
around the to the role of the use variation in the clinical out-
specific inj otocol could be o es tendinopathy (1,12).
importance on of the fluid after The primary purpose of the present study was to evaluate the effect of

Immobilization (+)

-prevent recurrent injury

-keep the injectate in place

Immobilization (-)

-early loading/

mecanotransduction

helpful for healing

YES, YOU HAVE TO DO YOUR REHAB

EVEN AFTER PRP

- N=130 rats
- PRP vs control (no injection)
- Activity cages vs normal cages
- Botox (unloaded tendon) vs no botox

- Results
- PRP tendons were >1/3 as strong as with normal loading
- Type of activity cage did not influence response to platelets
- Rats treated with botox lost all stimulatory effects of platelets

Acta Orthopaedica 2006; 77 (5): 806–812

How can one platelet injection after tendon injury lead to a stronger tendon after 4 weeks?

Interplay between early regeneration and mechanical stimulation

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5. Accepted 06-03-30

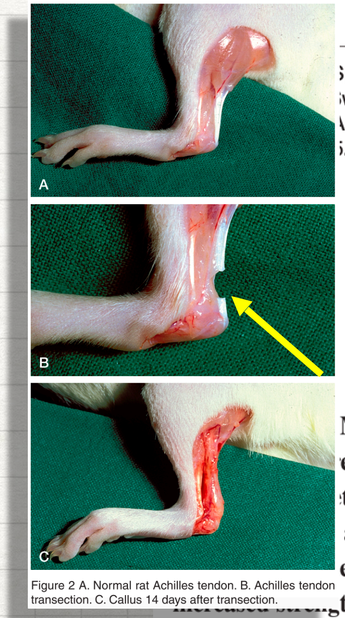

Figure 2 A. Normal rat Achilles tendon. B. Achilles tendon transection. C. Callus 14 days after transection.

Methods We studied the effects of platelets on Achilles tendon regenerates in rats 3, 5 and 14 days after transection. The tendons were either unloaded by *Botulinum* toxin A (Botox) injections into the calf muscles, or mechanically stimulated in activity cages. No Botox injections and ordinary cages, respectively, served as controls. Repair was evaluated by tensile testing.

Results At 14 days, unloading (with Botox) abolished any effect of the platelets and reduced the mechanical properties of the repair tissue to less than half of normal. Thus, some mechanical stimulation is a prerequisite for the effect of platelets at 14 days. Without Botox, both activity and platelets increased repair independently of each other. However, at 3 and 5 days, platelets improved the mechanical properties in Botox-treated rats.

Interpretation Platelets influence only the early phases of regeneration, but this allows mechanical stimulation to start driving neo-tendon development at an earlier time point, which kept it constantly ahead of the controls.

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WE KNOW WE NEED TO LOAD

BUT WHEN

- Systematic review- 84 studies
- Half limit activity for between 2-7 days
- Half initiate ROM/stretching at between 2-7 days post injection
- Over half initiate strengthening at 2-3 weeks post injection
- RTP between 4-6 weeks

Table 4
Most common timing for various PRP protocol elements

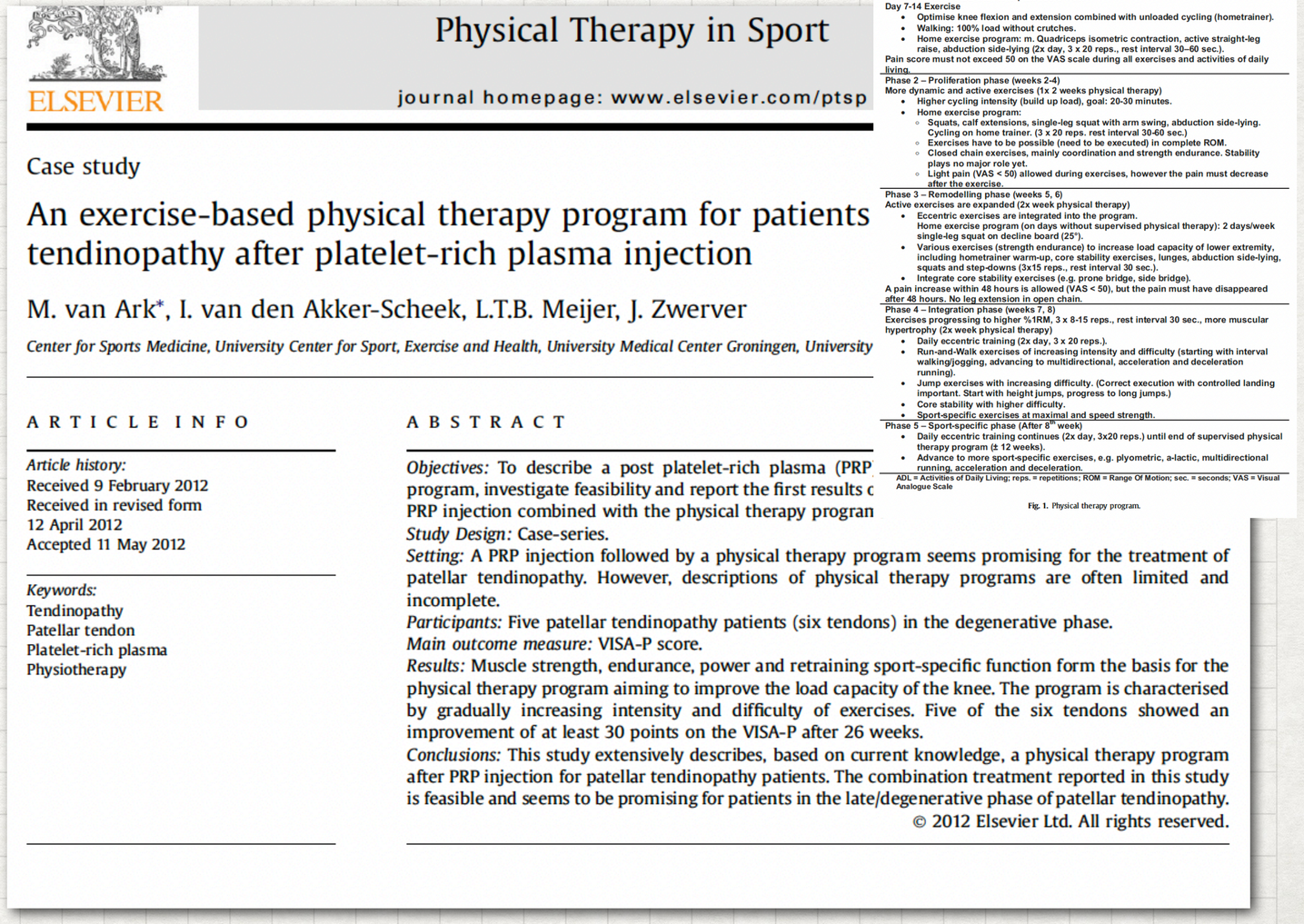
Protocol Element	Articles Mentioning Protocol Element (n, %)	Most Common Restricted Time Frame	Number of Protocols Recommending This Duration/Total Number of Protocols Providing Specific Data on This Protocol Element
Restrictions			
NSAIDs pre-PRP	17 (20%)	7-13 d	10/17
NSAIDs post-PRP	47 (56%)	>13 d	18/24
Weight bearing	10 (12%)	2-7 d	7/10
Orthosis/Crutches*	11 (13%)	>7 d	6/11
Activity limitation	42 (50%)	2-7 d	24/42
Initiation			
Range of motion/ stretching	43 (51%)	2-7 d	16/30
Strengthening	45 (54%)	14-21 d	25/33
Return to play	35 (42%)	4-6 wk	19/35

*For lower limb protocols only.
NSAID, nonsteroidal anti-inflammatory drug; PRP, platelet-rich plasma.

REHAB FOLLOWING PRP FOR PATELLA TENDON & OUTCOMES

A 5 STAGE PROGRAM

- n=5 (6 patella tendons)—arthrex prp
- 5 of 6 show improvement in VISA-P and patients would recommend this treatment to family/friends
- 1 patient did not show improvement and would not recommend- same patient had lowest self reported patient compliance
- 3 patients with the highest self reported compliance showed the largest improvement
- Eccentrics started at 5 weeks post prp



ELSEVIER

Physical Therapy in Sport

journal homepage: www.elsevier.com/ptsp

Case study

An exercise-based physical therapy program for patients tendinopathy after platelet-rich plasma injection

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Keywords:
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Patellar tendon
Platelet-rich plasma
Physiotherapy

ABSTRACT

Objectives: To describe a post platelet-rich plasma (PRP program, investigate feasibility and report the first results c PRP injection combined with the physical therapy progran
Study Design: Case-series.
Setting: A PRP injection followed by a physical therapy program seems promising for the treatment of patellar tendinopathy. However, descriptions of physical therapy programs are often limited and incomplete.
Participants: Five patellar tendinopathy patients (six tendons) in the degenerative phase.
Main outcome measure: VISA-P score.
Results: Muscle strength, endurance, power and retraining sport-specific function form the basis for the physical therapy program aiming to improve the load capacity of the knee. The program is characterised by gradually increasing intensity and difficulty of exercises. Five of the six tendons showed an improvement of at least 30 points on the VISA-P after 26 weeks.
Conclusions: This study extensively describes, based on current knowledge, a physical therapy program after PRP injection for patellar tendinopathy patients. The combination treatment reported in this study is feasible and seems to be promising for patients in the late/degenerative phase of patellar tendinopathy.

Phase 1 – Inflammation/proliferation phase (0-2 weeks)
Inform and advise patient, rest, low load (1x week physical therapy)
Day 1-3 Inform and advise patient
- Rest.
- Low load (walk with two crutches).
- Reduce pain (cryotherapy).

Day 4-7 Inform and advise patient
- Optimise ROM if necessary, combined with isometric exercises for m. Quadriceps.
- Increase ADL with VAS pain score < 50.

Day 7-14 Exercise
- Optimise knee flexion and extension combined with unloaded cycling (hometrainer).
- Walking: 100% load without crutches.
- Home exercise program: m. Quadriceps isometric contraction, active straight-leg raise, abduction side-lying (2x day, 3 x 20 reps., rest interval 30–60 sec.).

Pain score must not exceed 50 on the VAS scale during all exercises and activities of daily living.

Phase 2 – Proliferation phase (weeks 2-4)
More dynamic and active exercises (1x 2 weeks physical therapy)
- Higher cycling intensity (build up load), goal: 20-30 minutes.
- Home exercise program:
  - Squats, calf extensions, single-leg squat with arm swing, abduction side-lying. Cycling on home trainer. (3 x 20 reps. rest interval 30-60 sec.)
  - Exercises have to be possible (need to be executed) in complete ROM.
  - Closed chain exercises, mainly coordination and strength endurance. Stability plays no major role yet.
  - Light pain (VAS < 50) allowed during exercises, however the pain must decrease after the exercise.

Phase 3 – Remodelling phase (weeks 5, 6)
Active exercises are expanded (2x week physical therapy)
- Eccentric exercises are integrated into the program.
  Home exercise program (on days without supervised physical therapy): 2 days/week single-leg squat on decline board (25°).
- Various exercises (strength endurance) to increase load capacity of lower extremity, including hometrainer warm-up, core stability exercises, lunges, abduction side-lying, squats and step-downs (3x15 reps., rest interval 30 sec.).
- Integrate core stability exercises (e.g. prone bridge, side bridge).

A pain increase within 48 hours is allowed (VAS < 50), but the pain must have disappeared after 48 hours. No leg extension in open chain.

Phase 4 – Integration phase (weeks 7, 8)
Exercises progressing to higher %1RM, 3 x 8-15 reps., rest interval 30 sec., more muscular hypertrophy (2x week physical therapy)
- Daily eccentric training (2x day, 3 x 20 reps.).
- Run-and-Walk exercises of increasing intensity and difficulty (starting with interval walking/jogging, advancing to multidirectional, acceleration and deceleration running).
- Jump exercises with increasing difficulty. (Correct execution with controlled landing important. Start with height jumps, progress to long jumps.)
- Core stability with higher difficulty.
- Sport-specific exercises at maximal and speed strength.

Phase 5 – Sport-specific phase (After 8th week)
- Daily eccentric training continues (2x day, 3x20 reps.) until end of supervised physical therapy program (± 12 weeks).
- Advance to more sport-specific exercises, e.g. plyometric, a-lactic, multidirectional running, acceleration and deceleration.

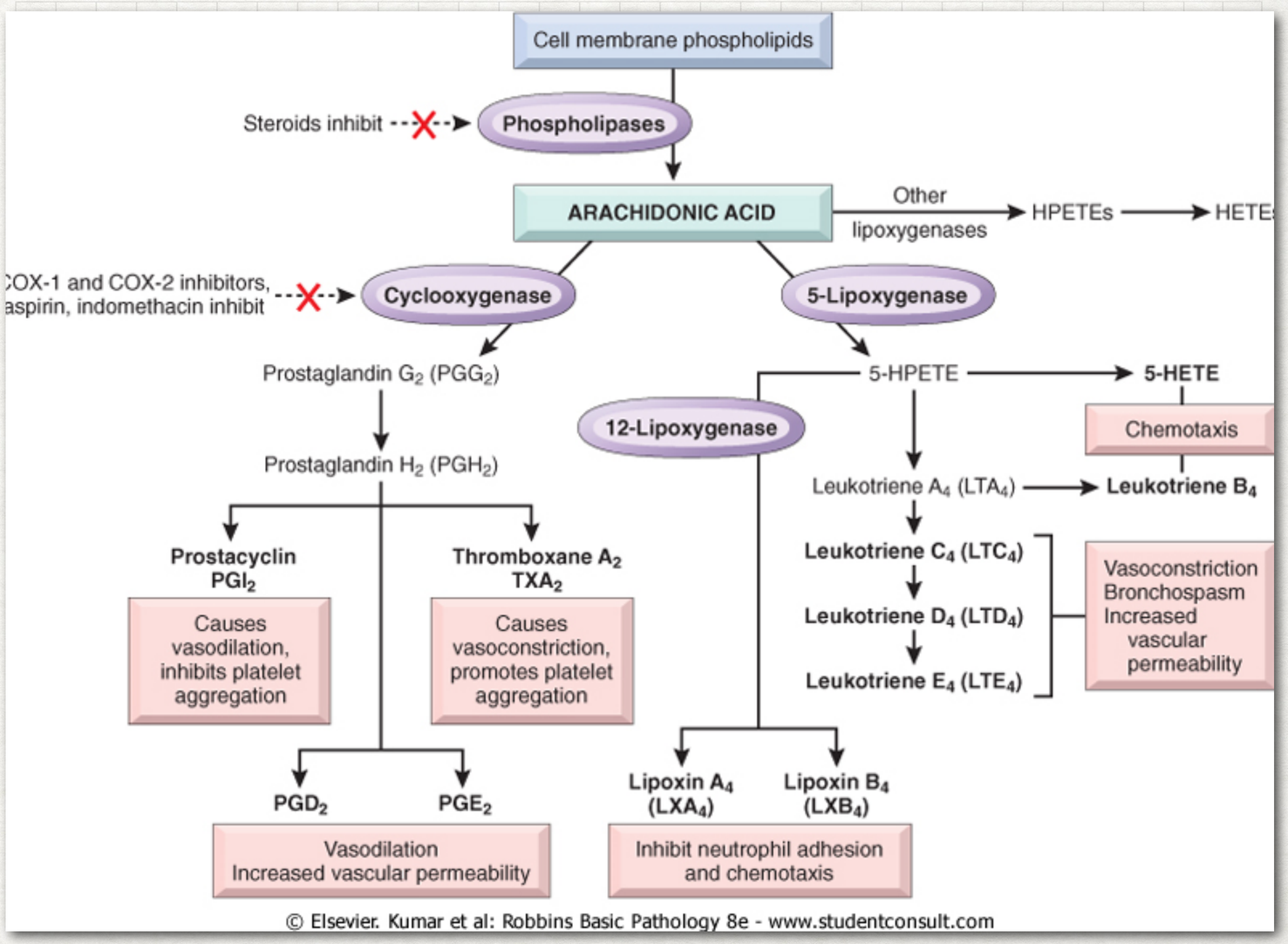
ADL = Activities of Daily Living; reps. = repetitions; ROM = Range Of Motion; sec. = seconds; VAS = Visual Analogue Scale

Fig. 1. Physical therapy program.

DO WE NEED TO STOP NSAIDS

PRE AND POST PRP

- Platelets live for an average of 5-10 days
- Many studies have shown NSAIDs may suppress positive physiological response to injury
- Aspirin inactivates platelets by acetylation of cyclooxyrgenase and decreased prostaglandin



DELPHI PRELIM RESULTS

ENROLLMENT

- 28 experts in the field—at least 500 PRP procedures preformed or rehabbed
- Average years of experience with PRP 12
- Average # of cases 1500
- Consensus considered: (strongly agree+ agree OR strongly disagree + disagree) at least 75% of respondents

PRE PROCEDURAL CONSIDERATIONS

WHAT REACHED CONSENSUS

- A restriction period is needed for reversible COX inhibitors (ibuprofen, naproxen, diclofenac, celecoxib) before PRP injection (agree)
  - mean # of days 8.75

- PRP can be preformed with the patient is on
  - traditional anti coagulants (e.g. heparin, Warfarin) (agree)
  - direct oral anticoagulants (DOACs) eg. Dabigatran, rivaroxaban, apixaban, or edoxaban) (agree)
  - statins (agree)
  - acetaminophen (agree)

- Failure of conservative management (such as PT or injections) is a contraindication (disagree)
- Active blood based malignancy is a contraindication (agree)
- PRP should not be preformed in close proximity to a local CSI @ the same location (agree)
  - Average time between csi and prp 47.9 days — 6.8 weeks
- PRP should be avoided in patients with an active infection (agree)
- PRP should be avoided in patients with stable autoimmune diseases (disagree)

PRE PROCEDURAL CONSIDERATIONS

NO CONSENSUS REACHED

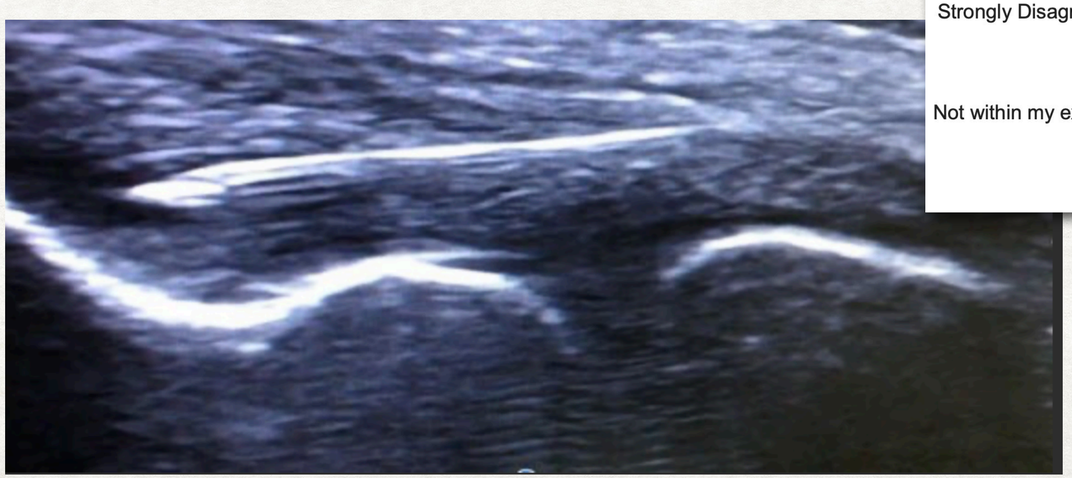
- A restriction period is needed for:
  - irreversible COX inhibitors (i.e. Aspirin)
  - anti-inflammatory supplements (i.e. Turmeric)
  - anti-oxidant supplements
  - Disease modifying anti-rheumeatics (DMARDs)

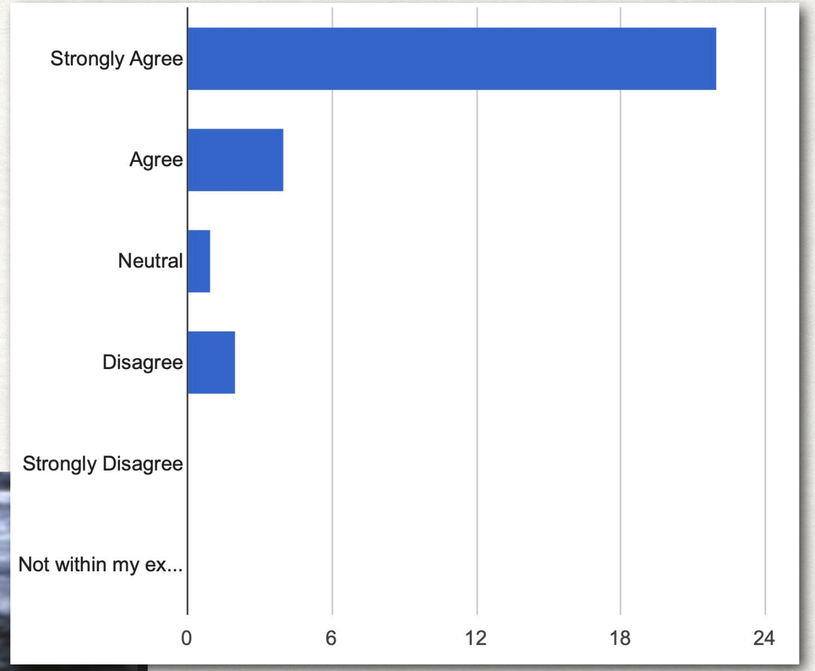
- Low dose aspirin (81mg) used for cardiovascular or cerebrovascular prevention may be continued before PRP
- PRP can be preformed while the patient is on anti platelet meds (ie clopidogrel)
- An active non blood based malignancy is a contraindication to PRP
- A history of blood based malignancy is a contraindication to PRP
- A history of a non blood based malignancy is a contraindication to PRP
- PRP should not be performed in close proximity to a local csi @ a different location
- PRP should not be performed in close proximity to a systemic corticosteroid (i.e prednisone)
- PRP should be avoided in patients with
  - active bleeding disorders (hemophilia)
  - active autoimmune disease
  - during pregnancy

PERI PROCEDURAL CONSIDERATIONS

WHAT REACHED CONSENSUS

- Image guidance (US or fluoro) should be used to ensure accurate delivery (agree)

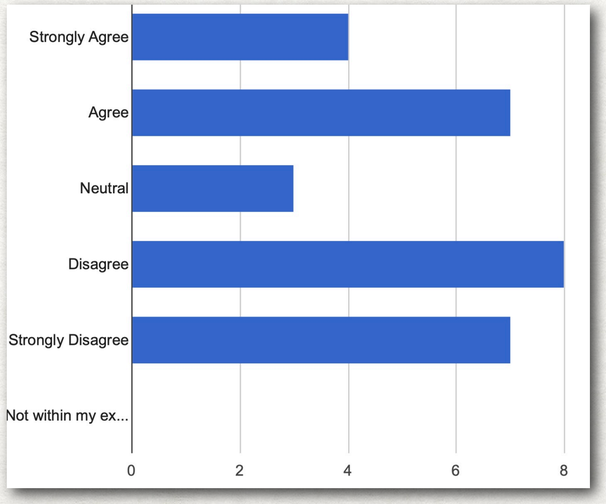




PERI PROCEDURAL CONSIDERATIONS

NO CONSENSUS REACHED

- Local anesthetics should not be mixed with the PRP in the same syringe
- For tendon pathology, local anesthetics should not be injected into the tendon
- For OA local anesthetics should not be injected intra-articularly alongside PRP
- Landmark guided PRP are acceptable in experienced hands and specific clinical scenarios



POST PROCEDURAL CONSIDERATIONS

WHAT REACHED CONSENSUS

- NSAIDs should be avoided following PRP (agree) (mean 14 days)
- Following PRP, a period of rest should be considered before intiating PT
    - Mean of 8.48 days (SD 8.98) for OA and mean of 10 days (7.98 SD) for tendon
  - How many days of bracing/offloading for soft tissues around the
    - Knee joint- mean 16
    - Foot/ankle- mean 12
  - Days of immobilization and/or WB restriction for soft tissue around knee joints—mean 9 days
  - Days of immobilization for soft tissue around foot/ankle—mean 10.44 days
  - Post procedural rehab should begin with stretching and AROM without active load and progress to isometric, concentric, eccentric, and plyometric at the discretion of the PT (agree)

POST PROCEDURAL CONSIDERATIONS

NO CONSENSUS REACHED

- Differences in OA severity/stage should be considered when guiding post procedural rehab
- Ice/cryotherapy should be avoided following PRP
- More than one PRP is recommended for the treatment of OA
- Progressive return to activity timelines should be standardized according to the underlying pathology and injection sites
- Progressive RTP/sport should be standardized based on pathology and injection sites

COMBINATION THERAPIES

WHAT REACHED CONSENSUS

- Shockwave therapy can be performed before or after PRP (agree)
- What interval, in days would you recommend b/w PRP and shockwave-mean 10 days

COMBINATION THERAPIES

NO CONSENSUS REACHED

- In cases where both PRP and shockwave are used PRP should be before or after
  - 44% of respondents said no preferred order
  - Laser/photobiomodulation therapy can be performed before or after PRP
  - Dry needling can be performed before or after PRP
  - Manual therapy of the adjacent muscles/soft tissue can be performed before or after PRP (72% agree)

THANK YOU!