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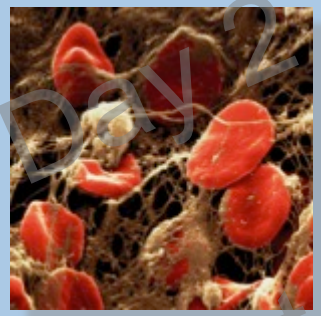
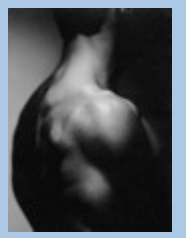
Scientific Principles of Rotator Cuff Repair: Biology?



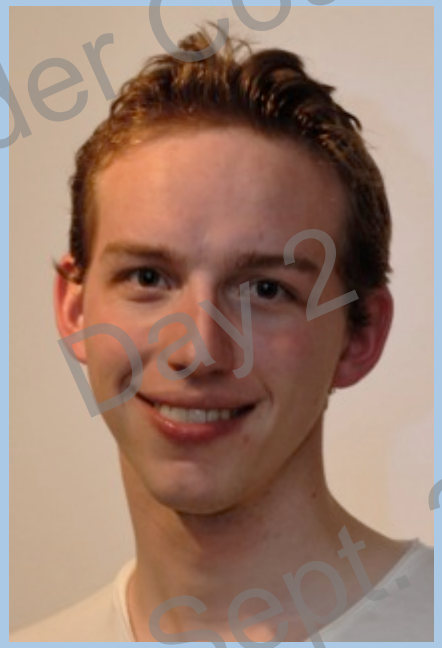
MA Zumstein
Shoulder, Elbow & Orthopaedics Sports Medicine
Department of Orthopedic Surgery and Traumatology
University of Berne, Switzerland
www.shoulderteam.ch



TOP TEAM

TOP TEAM: TOP COLLABORATORS

B. Moor



M. Kuenzler

M. Schaer

BIOLOGIC FACTORS THAT INFLUENCE...

- ..the origin of a tear

- ...the healing rate after repair

FACTORS

Extrinsic

Intrinsic

to the muscotendinous chain

BIOLOGIC FACTORS THAT INFLUENCE...

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- **Age of the patient**

Yamaguchi K, JBJS A: 2006
Galatz L, JBJS A: 2006
Boileau P, JBJS A: 2005
Lichtenberg S, KSSTA, 2006

BIOLOGIC FACTORS THAT INFLUENCE...

- Age of the patient
- **Smoking**

Mallon WJ, JSES A: 2004

BIOLOGIC FACTORS THAT INFLUENCE...

- Age of the patient
- Smoking
- **NSAID**

NSAID decreases the ultimate load to failure

Cohen DB, AJSM: 2006

BIOLOGIC FACTORS THAT INFLUENCE...

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- Age of the patient
- Smoking
- NSAID
- **Diabetes mellitus**
- **Hypercholesterolinemia**

Bedi A et al. JSES, 2010

Abboud et al., Clin Orthop Rel Research, 2010

BIOLOGIC FACTORS THAT INFLUENCE...

- Age of the patient
- Smoking
- NSAID
- Diabetes mellitus
- Hypercholesterolinemia
- **Vit. D deficiency**

Angeline ME et al. AJSM, 2014

BIOLOGIC FACTORS THAT INFLUENCE...

- Age of the patient
- Smoking
- NSAID
- Diabetes mellitus
- Hypercholesterolinemia
- Vit. D deficiency
- **Fluoroquinolones**

Fox AJ, Schaer M et al. AJSM, 2014

FACTORS THAT INFLUENCE THE HEALING RATE

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« Shoulder Course »

Day 2

12. Sept. 2014

Extrinsic

Intrinsic

to the muscotendinous chain

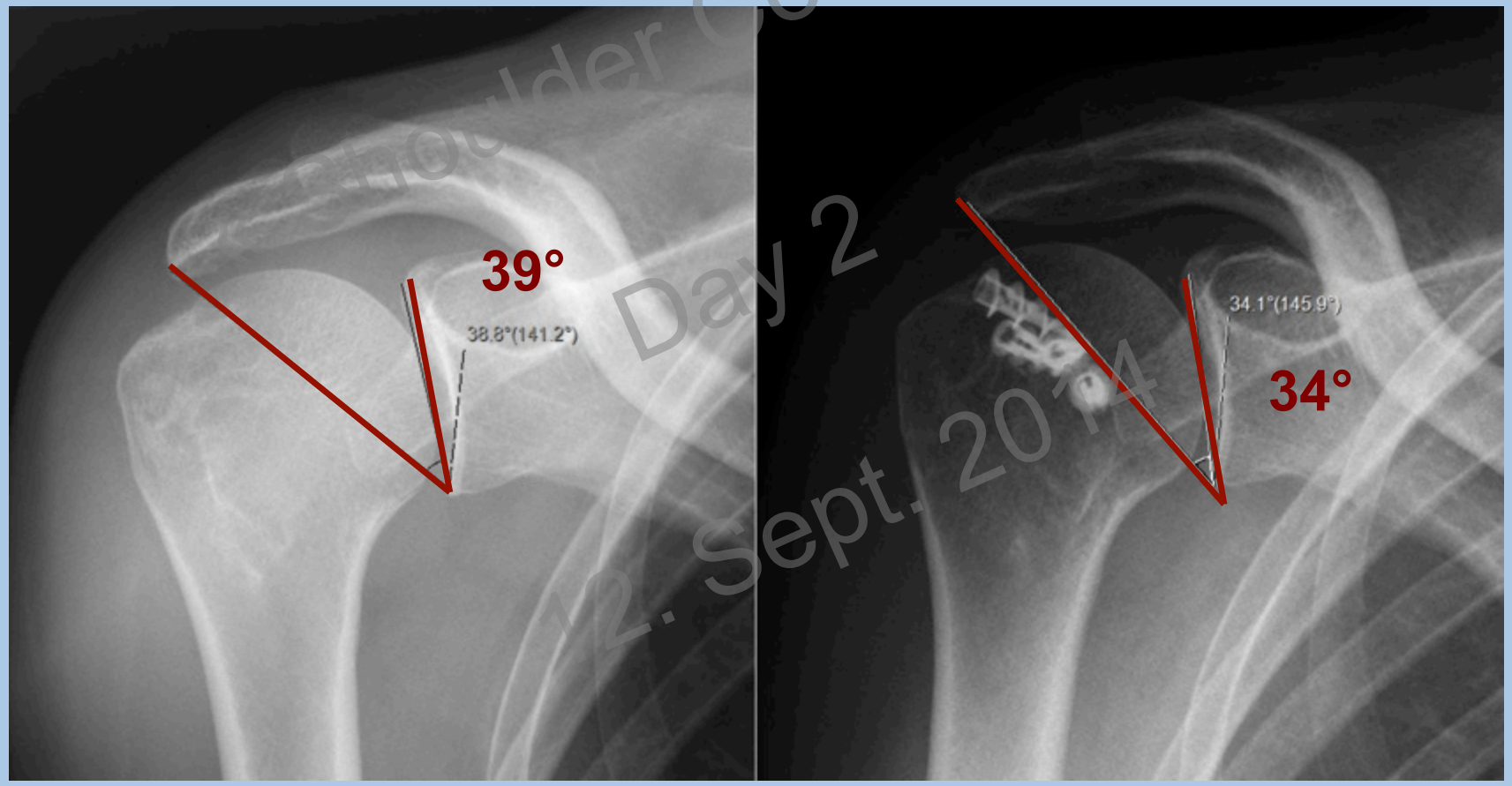
BIOLOGIC PROPERTIES

1. Bone
2. Insertion & tendon
3. Muscle

BIOLOGIC PROPERTIES

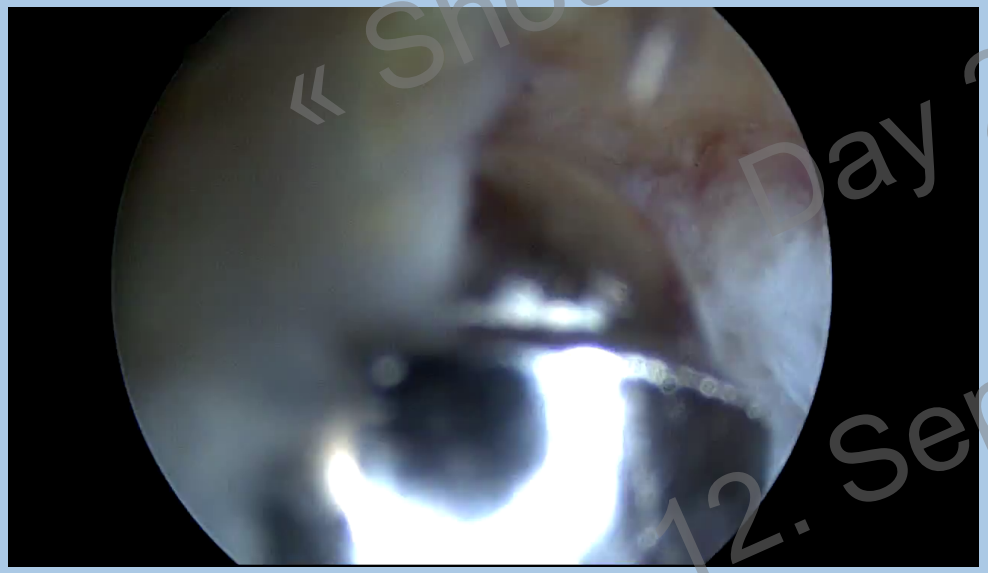
1. Bone
2. Insertion & tendon
3. Muscle

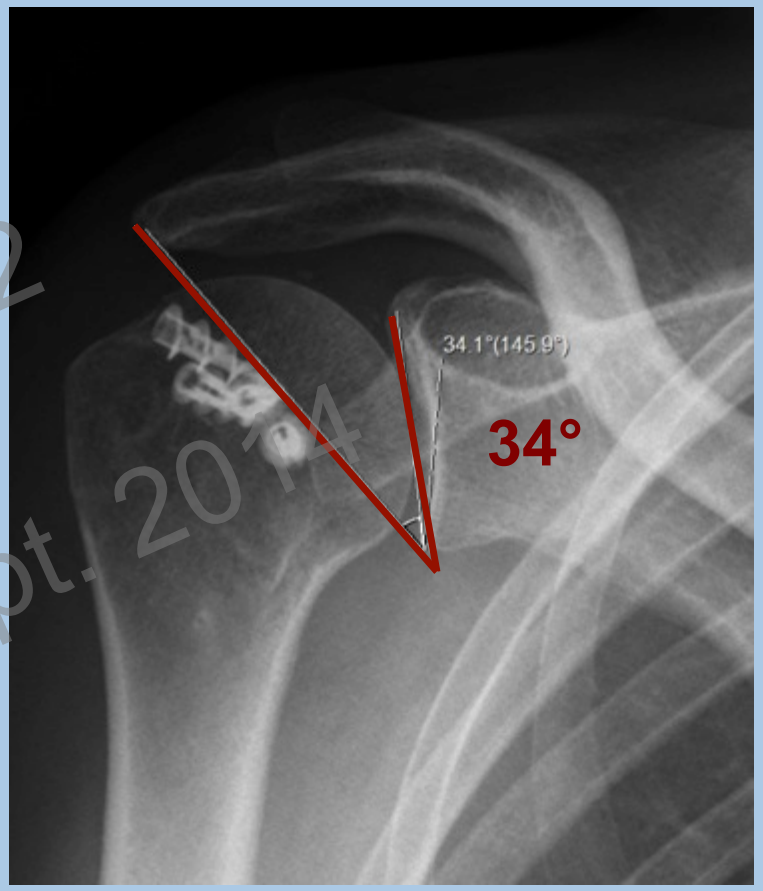
BONE MORPHOLOGY: CRITICAL SHOULDER ANGLE



Moor BKM et al. BJJ, 2013

BONE MORPHOLOGY: CRITICAL SHOULDER ANGLE





BONE QUALITY IN TEARS VS INTACT CUFFS IN MICRO CT

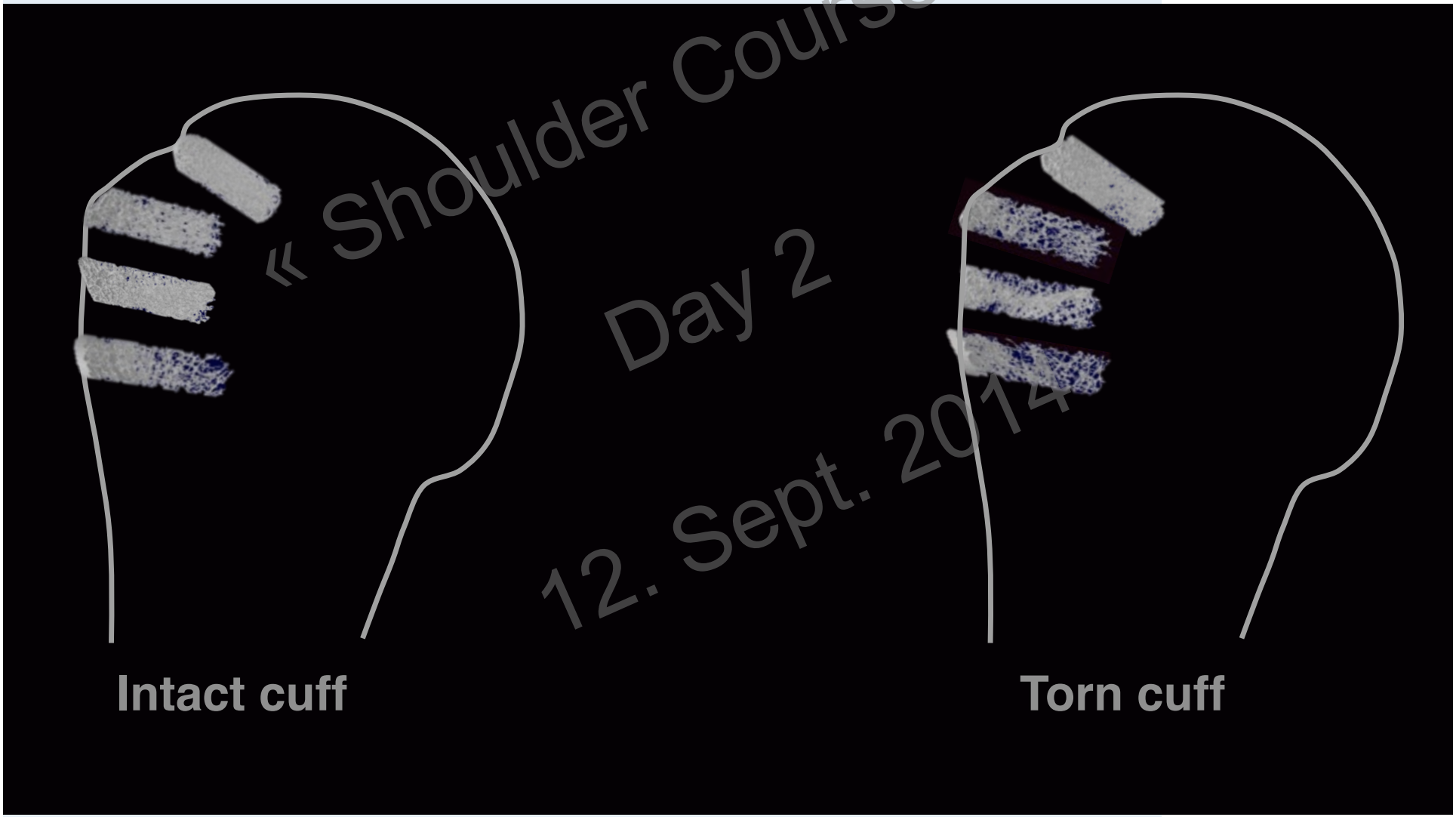
1. **Bone volume**
   - BV
   - BV/TV
2. **Bone Surface Properties**
   - Surface (=BS)
   - Turnover (=BS/BV)
   - Mech Properties (=BV/TV)
3. **Trabecular structures**
   - Latticies (=TbPf)
   - Rods & plates in 3D (SMI)
   - Trab. thickness (=TbTh)
   - Trab. number (=TbN)

Meyer DC et al. JSES, 2004

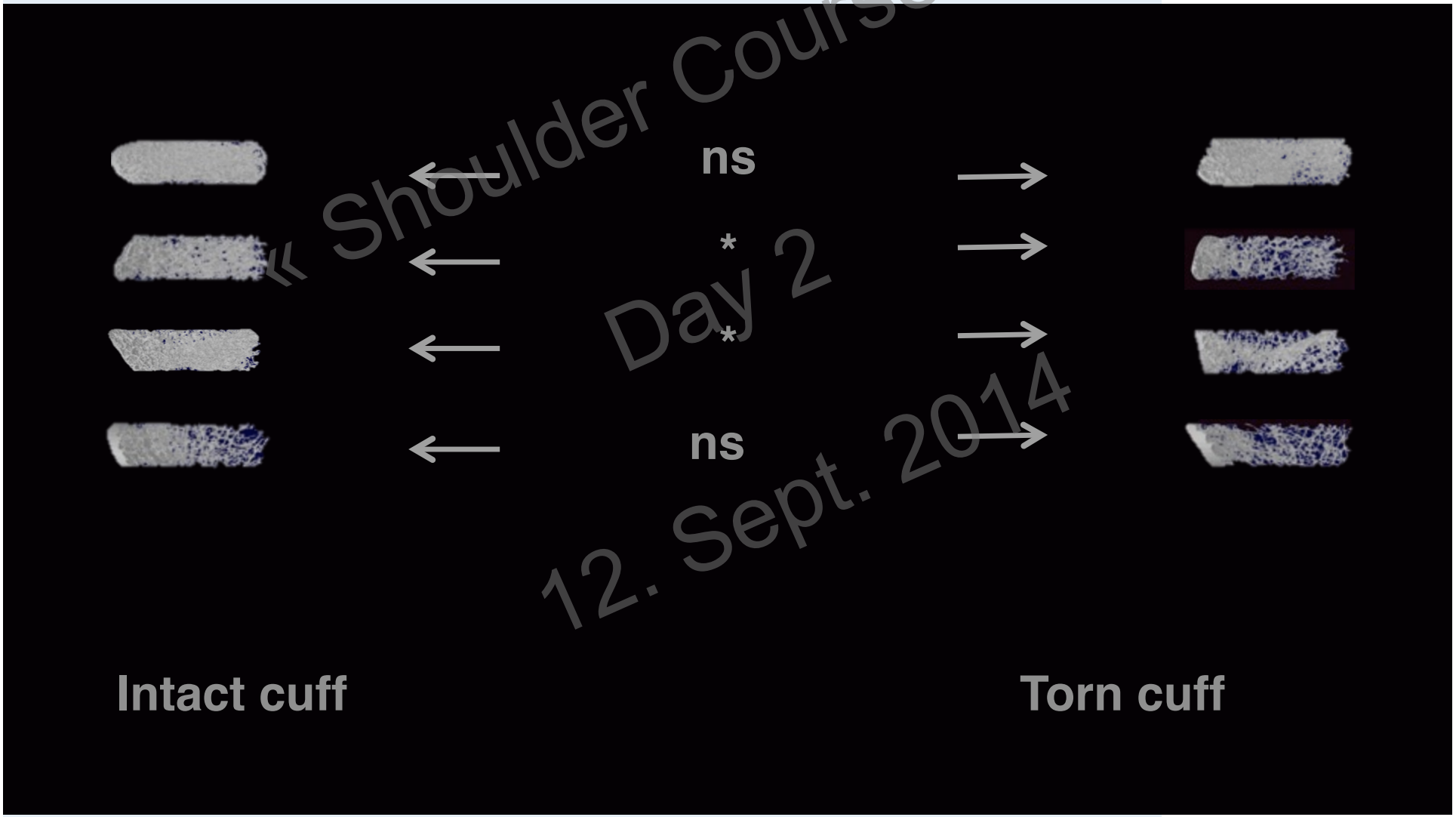
BEST BONE QUALITY ?
MICRO CT

THE UNIVERSITY OF ADELAIDE AUSTRALIA

UNIVERSITÄT BERN



BEST BONE QUALITY ?
MICRO CT



BEST BONE QUALITY ?
MICRO CT

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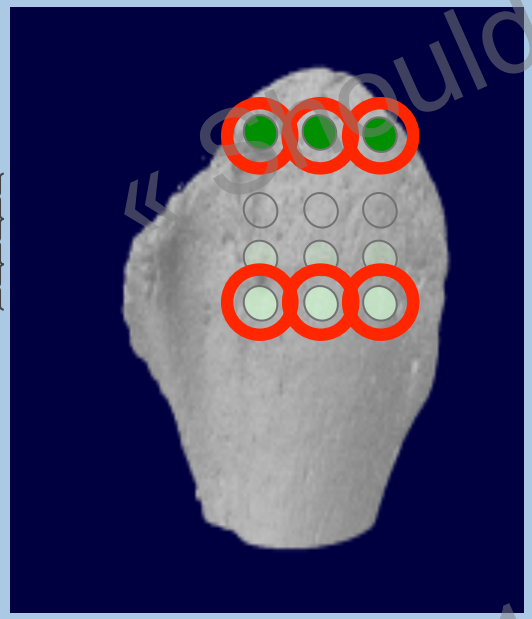
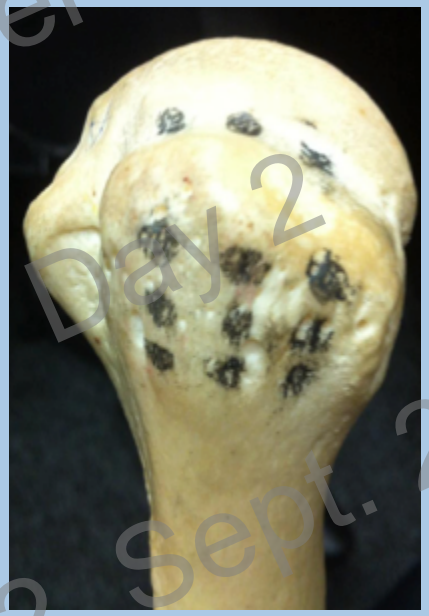
5 mm
10 mm
15 mm





BIOLOGIC PROPERTIES

1. Bone
2. **Insertion & tendon**
3. Muscle

PROPERTIES NATURAL INSERTION

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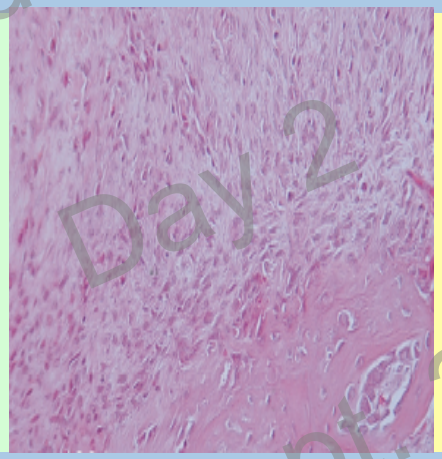
TENDON **FIBROCARTILAGE** **BONE**

ZONE I



ZONE IV

Woo SL. CORR: 1999

Galatz LM, J Orthop Res: 2006

Thomopoulos S, J Orthop Res: 2002

BIOLOGIC AUGMENTATION OPTIONS TODAY

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- **CELLS:**
  - **„stem“-progenitor-cells**
- **REGULATORS**
  - Cytokines, growth factors
  - Pharmacological products

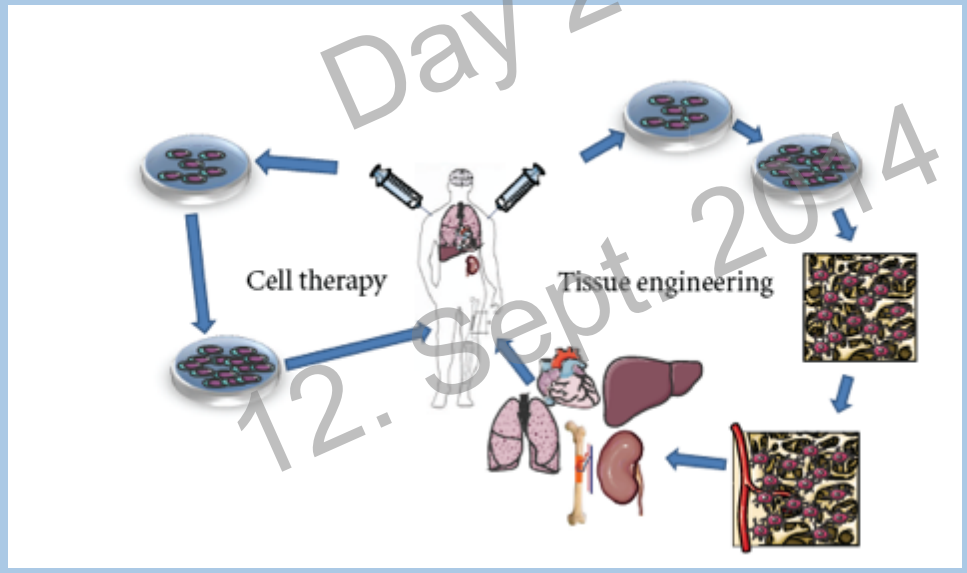
STEM CELL TREATMENT

Cell therapy

Cells were injected into tissue

Cell tissue engineering

Cells seeded on an matrix and differentiated through signal



Schmitt A, Stem Cell Int: 2012

STEM CELL TREATMENT

UNIVERSITÄT BERN

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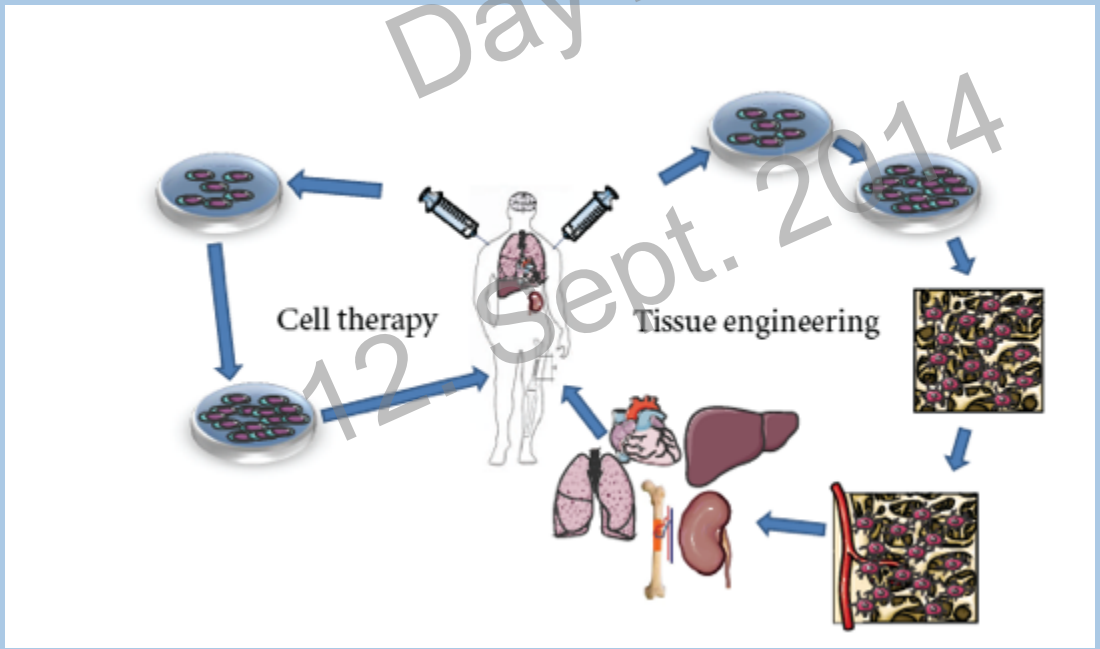

„YOUNG“ ADULT MSC THERAPY

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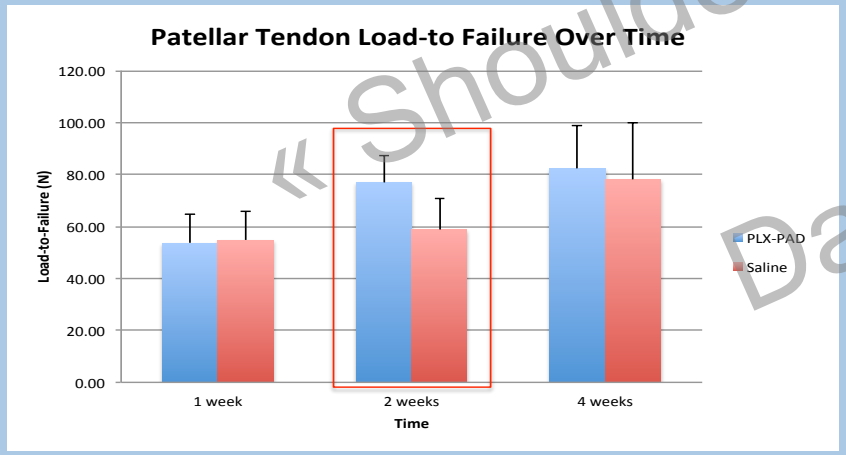
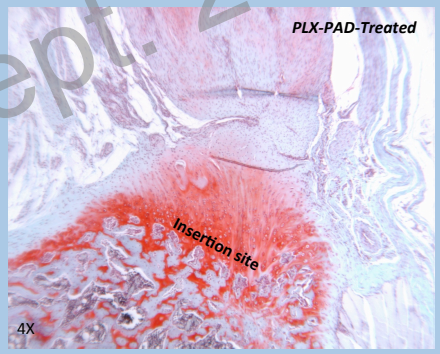
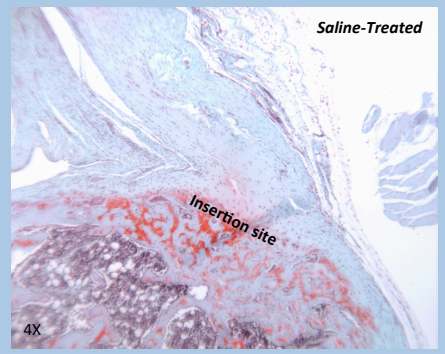
- **Placenta Derived Stem Cell Therapy**



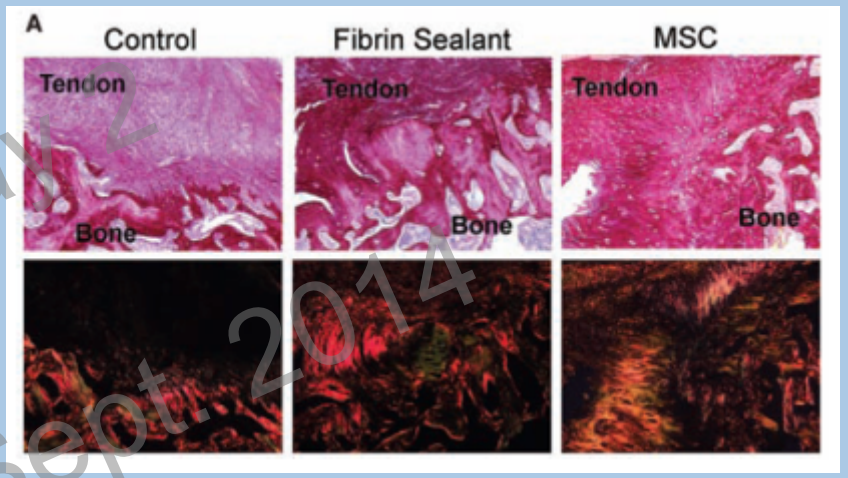




Ma, Schaer, Rodeo; unpublished data

„OLDER“ ADULT MSC THERAPY IN THE ROTATOR CUFF TENDON INSERTION

... did not improve the structure, composition, or strength of the healing tendon attachment site in rats



CAVE acute tear!

Gulotta LV, AJSM: 2009

STEM CELL TREATMENT

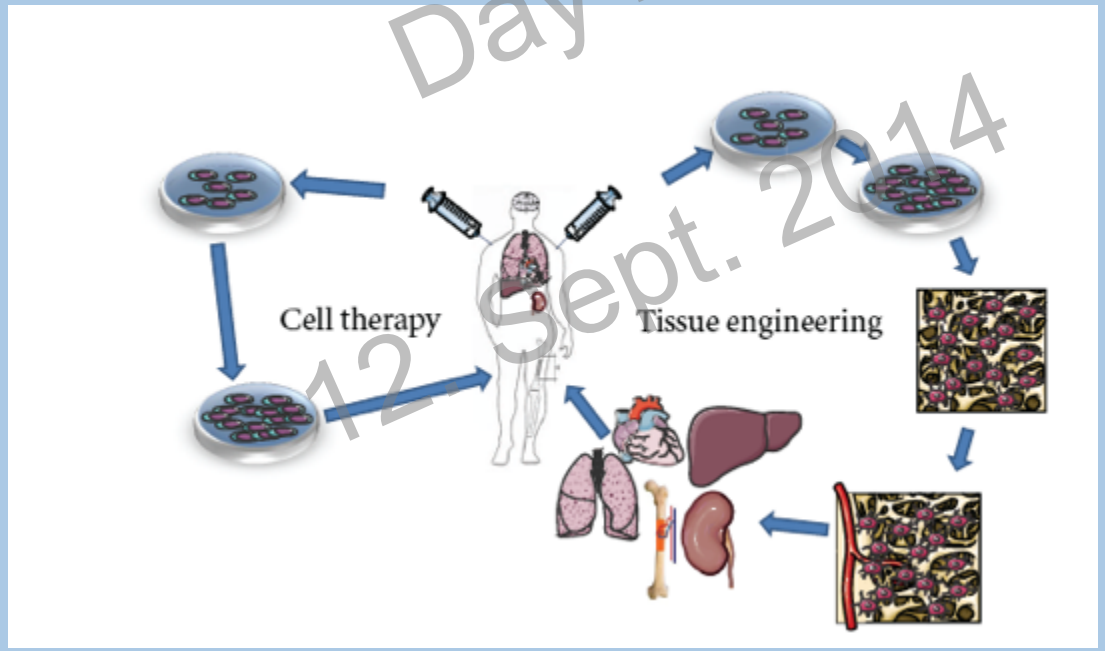
UNIVERSITÄT BERN

Cell therapy

Cells were injected into tissue

Cell tissue engineering

Cells seeded on an matrix and differentiated through signal



MSC TISSUE ENGINEERING
TRANSFECTION OF STEM CELLS

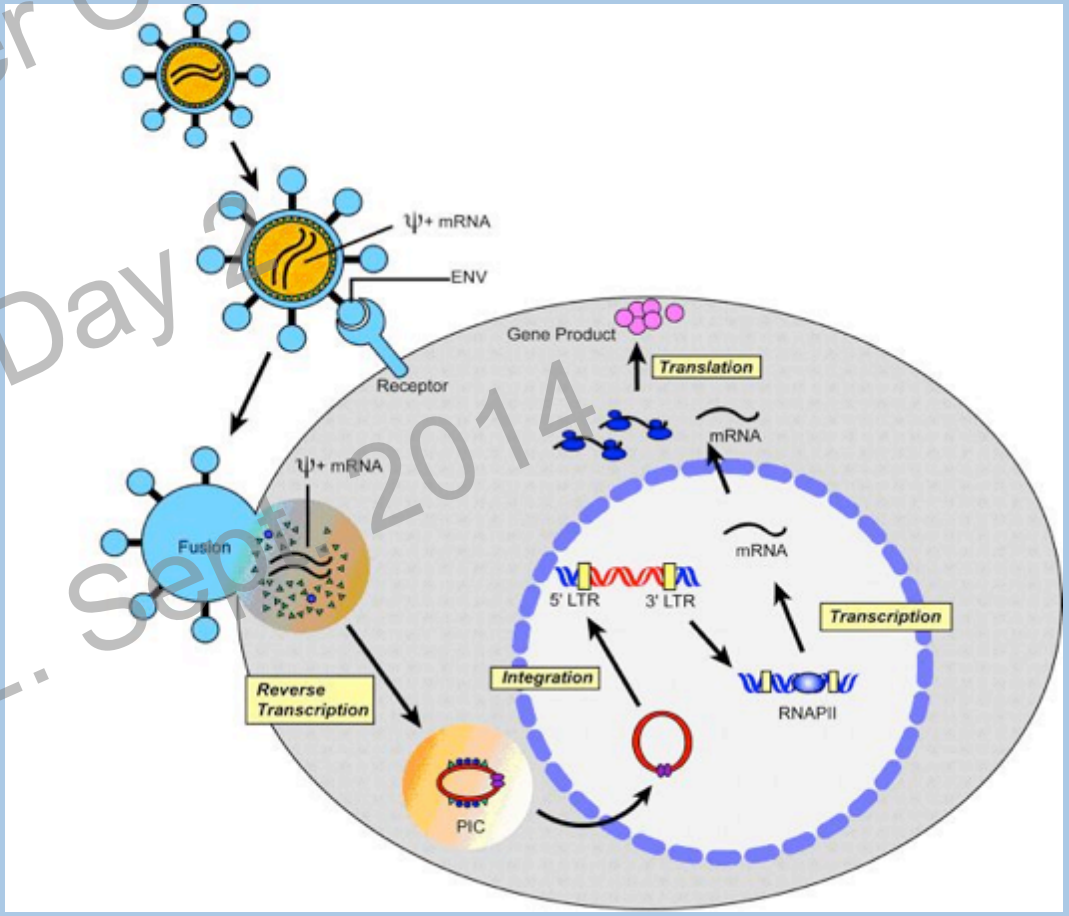
UNIVERSITÄT BERN

MSC

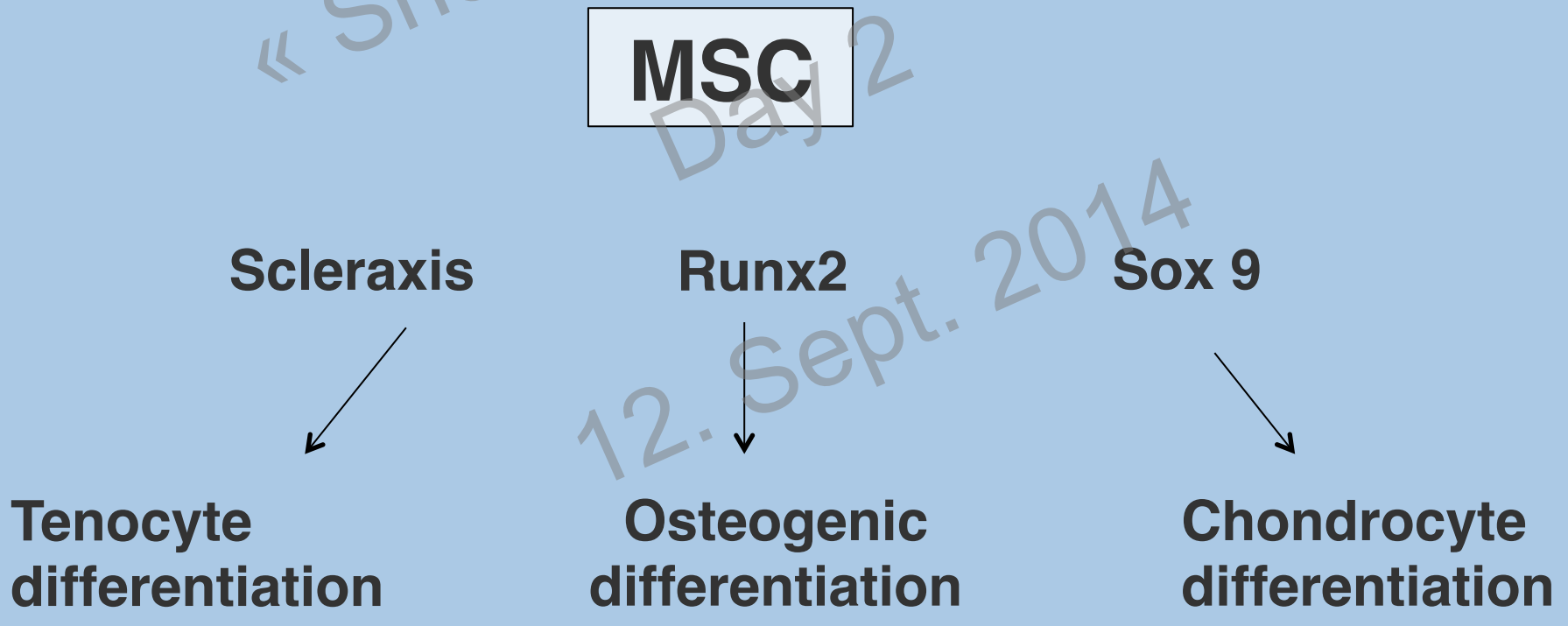
Virus

↓

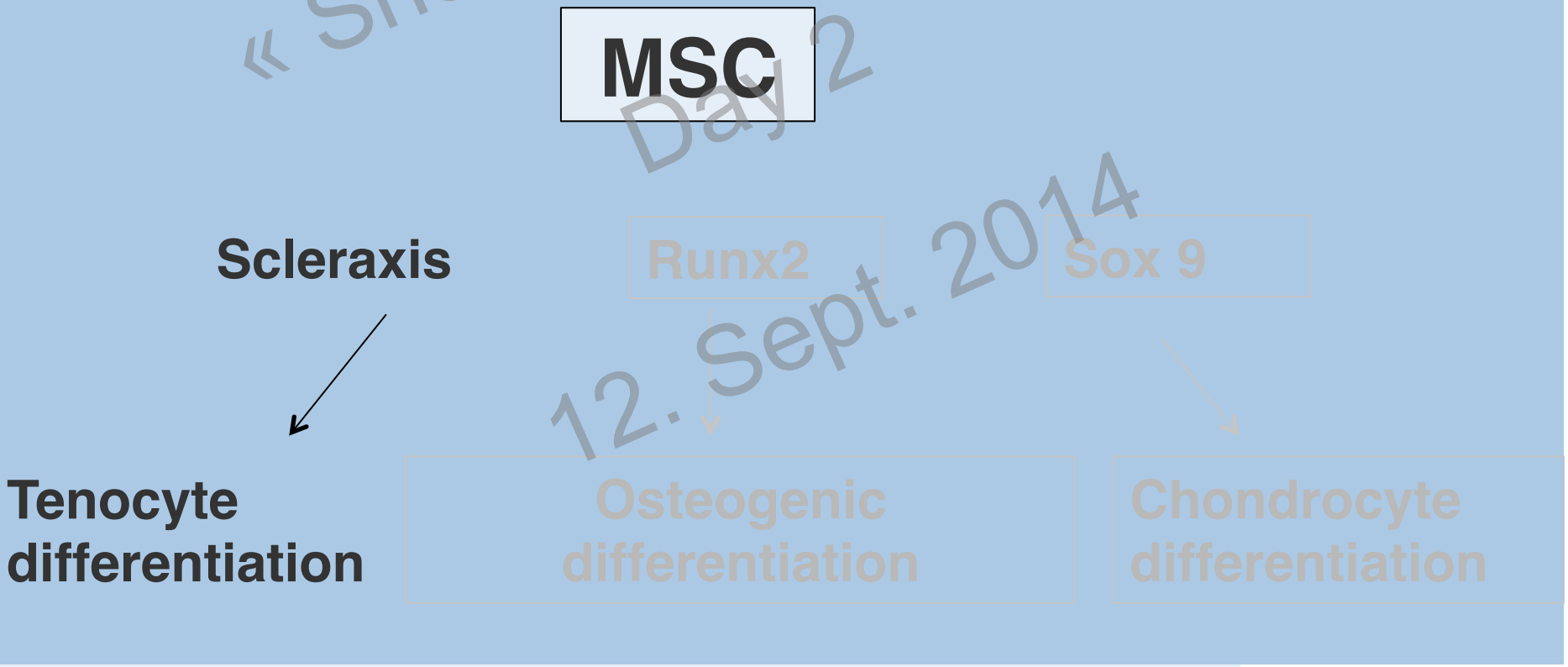
overexpression of proteins



EMBRYOLOGIC TENDON BONE HEALING



MSC TISSUE ENGINEERING FOR EMBRYOLOGIC TENDON BONE HEALING

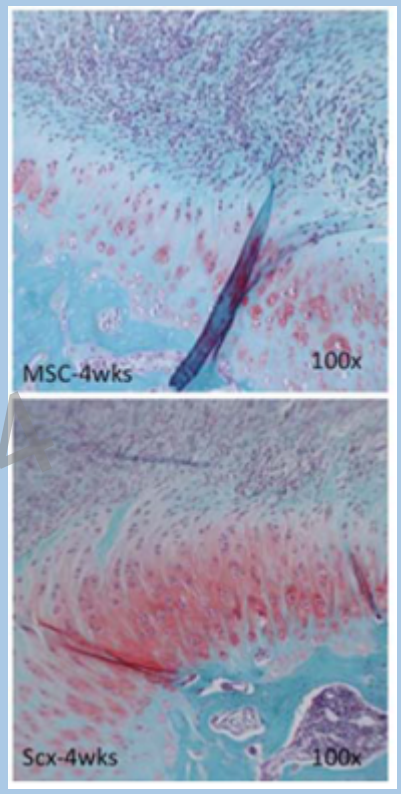


MSC TISSUE ENGINEERING INDUCE EMBRYOLOGIC PATHWAY

UNIVERSITÄT BERN

Scleraxis (SCX) transduced MSC's

- **... a significantly improved histologic outcome**
- **Increased fibrocartilage**
- **greater strength at the tendon-bone insertion site at 4 weeks**
- **less than normal insertion**



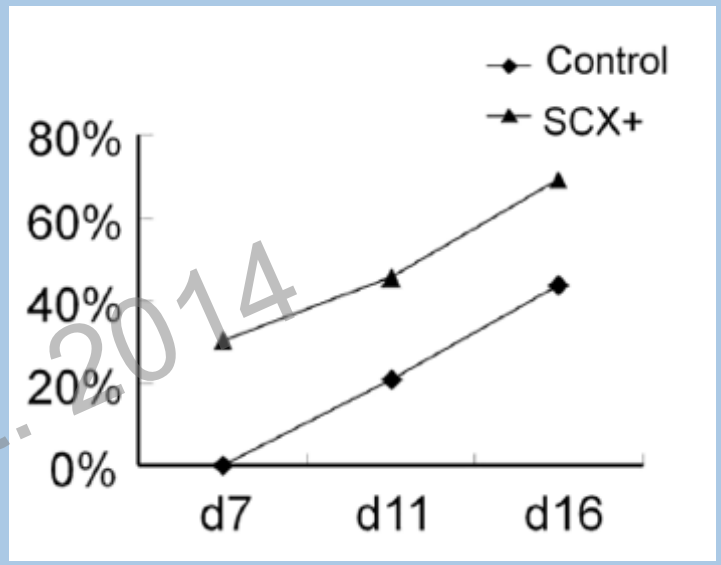
- **CAVE acute tear!**

Gulotta LV, AJSM: 2011

MSC TISSUE ENGINEERING INDUCE EMBRYOLOGIC PATHWAY

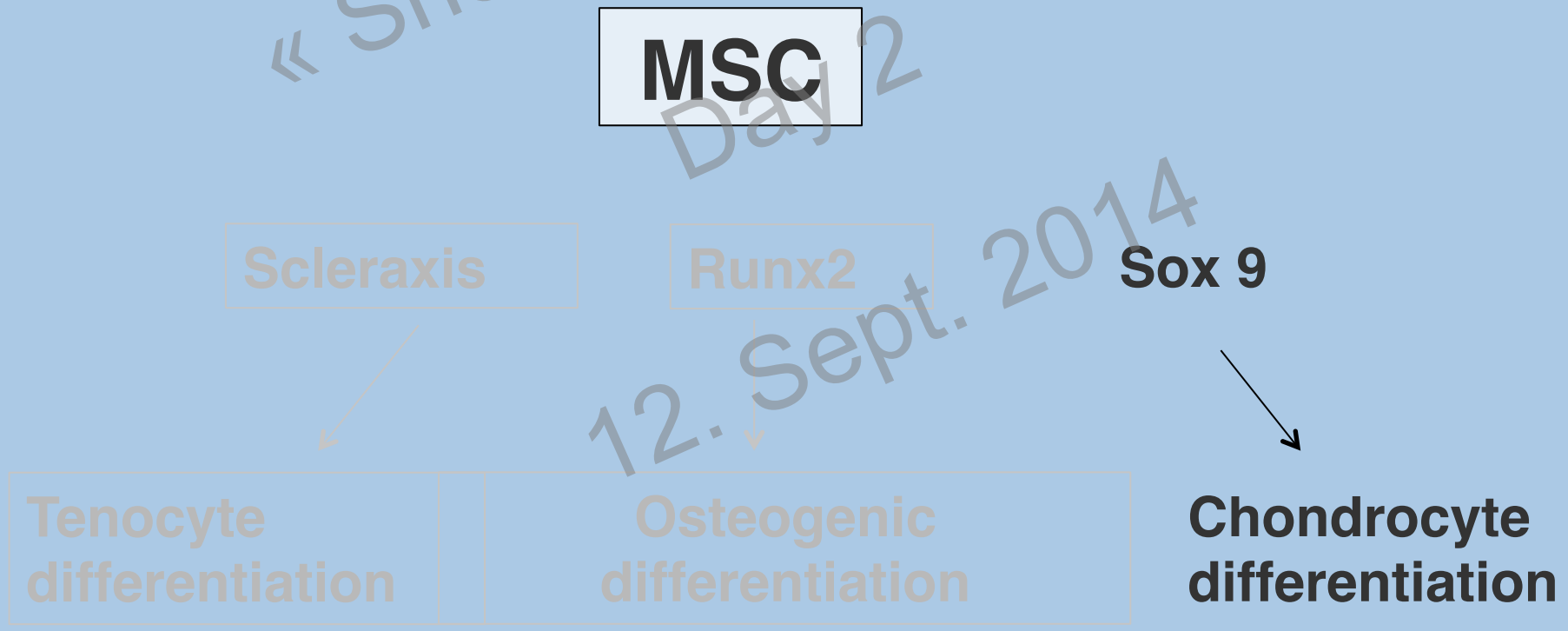
SCX induced MSC‘s coupled with force transmission

- **SCX augments <u>differentiation</u> of MSC‘s into tenocytes**
- **... synergistically promotes tendon <u>maturation</u>**



Chen X, Nature: 2012

MSC TISSUE ENGINEERING FOR EMBRYOLOGIC TENDON BONE HEALING



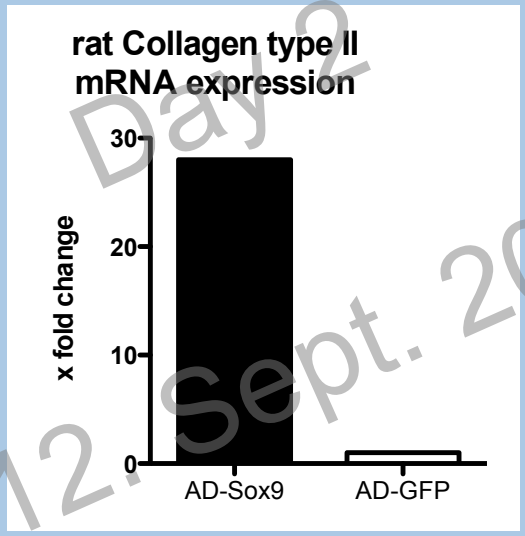
MSC TISSUE ENGINEERING
TRANSFECTION OF STEM CELLS

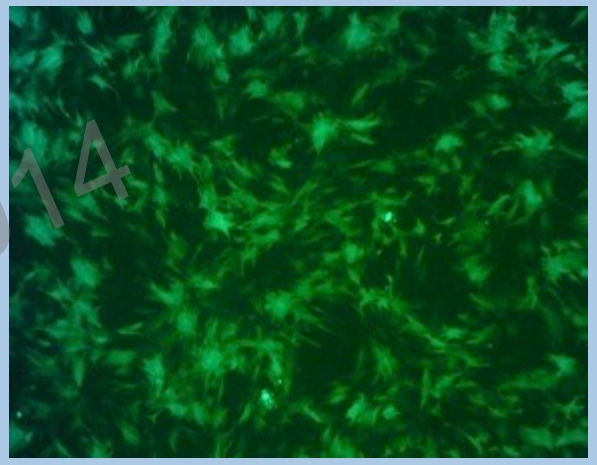
MSC

Virus

↓

overexpression of proteins





Schaer M, unpublished data: 2014

MSC TISSUE ENGINEERING
TRANSFECTION OF STEM CELLS

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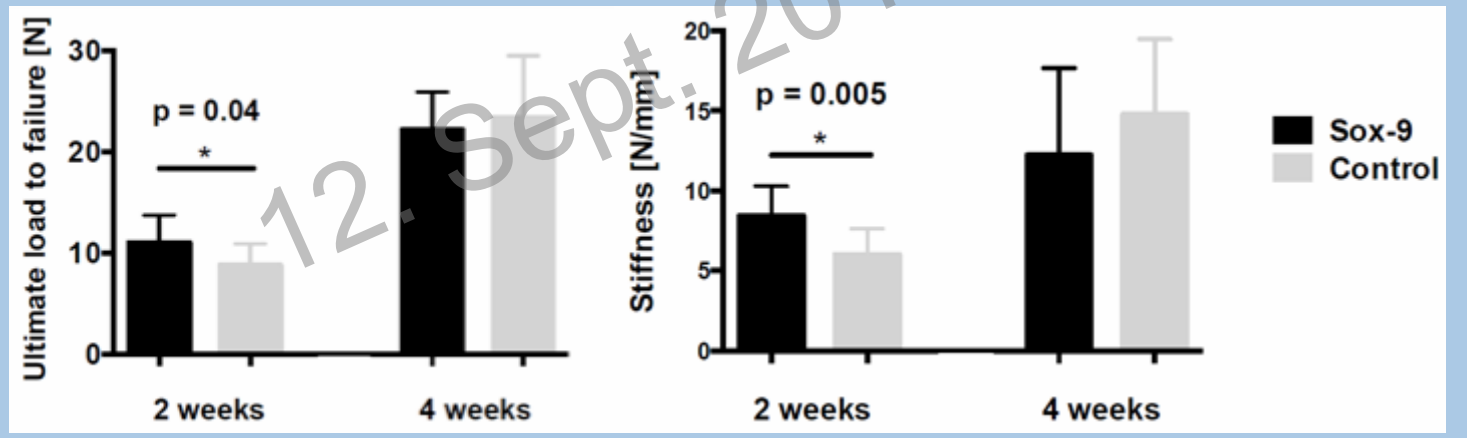
MSC

Virus

↓

overexpression of proteins



Schaer M, unpublished data: 2014

BIOLOGIC AUGMENTATION OPTIONS TODAY

- **CELLS:**
  - **„stem“-progenitor-cells**
- **REGULATORS**
  - **Cytokines, growth factors**
  - **Pharmacological products**

PLATELET ± LEUCOCYTE CONCENTRATES: CLASSIFICATION

Pure-Platetet-rich Plasma (P-PRP)	Platelet-Leukocyte-rich Plasma (L-PRP)	Pure Platelet-rich Fibrin (P-PRF)	Leukocute and Platelet-rich Fibrin (L-PRF)
Autologous Conditoned Plasma (ACP™) Arthrex Inc.	SmartPreP®2 Harvest Technologies	Cascade® Musc Transpl Foundation	Choukroun's PRF
Preparation Rich in Growth Factors (PRGF) Biotechn. Institute	GPS® III Biomet Biologics	PRGF Scaffold Biotechnology Institute	
	Magellan™ Arteriocyte Medical Systems	FIBRINET® PRFM Cascade Medical	
	Symphony™ II Depuy		
	Platelet Concentrate Collection System (PCCS® II)		
	Angel® Sorin Group		
	GenesisCS EmCyte		
	Cell Saver® 5 Haemonetics		

Dohan DM, Trends Biotech: 2010

Zumstein MA, Op Tech Sports Med: 2011

CONCLUSION PLATELET CONCENTRATES

- No scientific benefit of L-PRF

  Zumstein MA, JSES: 2014

- No scientific benefit of P-PRF

  Castricini R, AJSM: 2011 Rodeo S, AJSM: 2012

- Some scientific benefit of L- PRP?

  Randelli P, JSES: 2010 Gumina S, JBJS Am: 2012

- Some scientific benefit of P- PRP

  Jo CH, AJSM: 2011 Jo CH, AJSM: 2013

COCHRANE DATABASE

THE COCHRANE COLLABORATION®

UNIVERSITÄT BERN

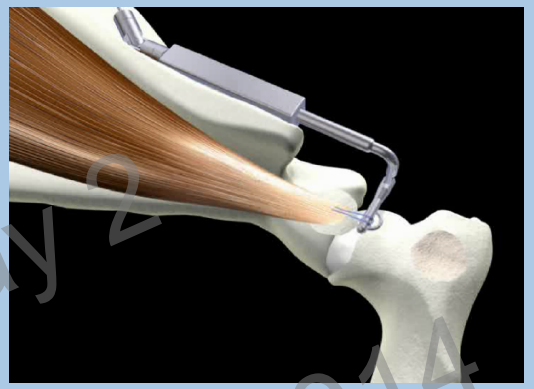
.... insufficient evidence to support the use of Platelet-rich therapies for treating musculoskeletal soft tissue injuries.

-> There is need for standardisation of PRP preparation methods.

Moares VY, Cochrane Database Sys Rev: 2014

PHARMACOLOGICAL PRODUCTS

- **Mechanical stimulation reduced tissue degeneration**



Gerber C, JSES: 2009

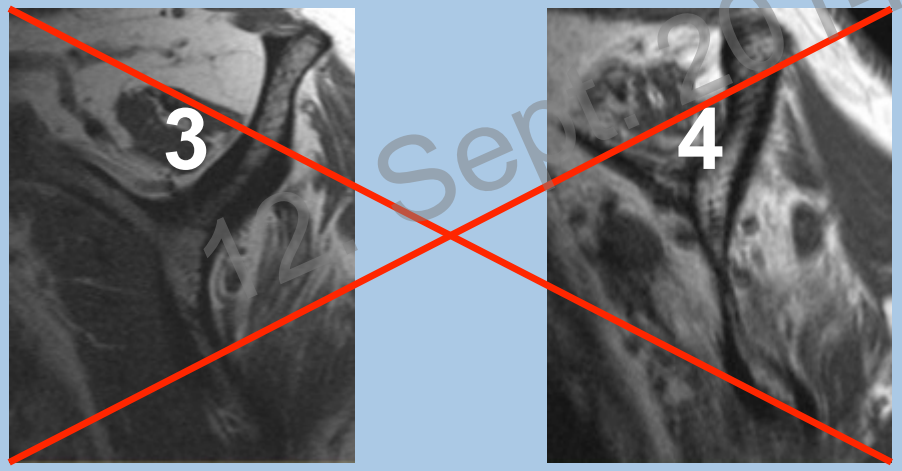
- **Pharmacological use of nandrolone or IGF does not improve tendon quality**

Wieser K, KSSTA: 20014

BIOLOGIC PROPERTIES

1. Bone
2. Insertion & tendon
3. **Muscle**

MUSCLE ATROPHY AND FATTY INFILTRATION



Goutallier D, CORR: 1994

REVERSIBILITY OF MUSCLE ATROPHY AND FATTY INFILTRATION

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Goals:

A. Reversion of architecture √
B. Stereoids prevented fatty infiltration √
C. Decrease of fat and connective tissue X
D. Hypertrophy of muscle substance X

Gerber C, Zumstein MA, JSES: 2009
Gerber C, JBJS Am: 2011
Frey E, Zumstein MA et al, JOR: 2009
Schmutz S, Zumstein MA et al. CORR: 2008

ADIPOSE DERIVED STEM CELLS (AD-MSCs) THERAPY

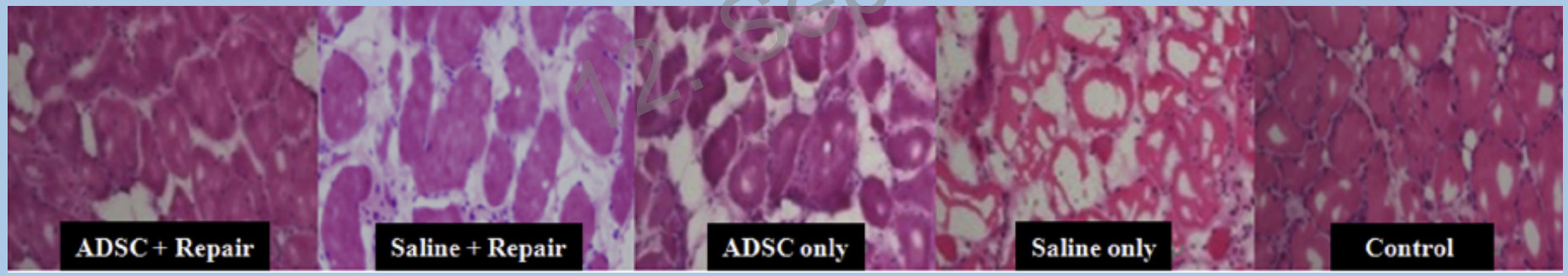
UNIVERSITÄT BERN

- chronic tear model
- Rabbits‘ SSC
- Injection of AD-MSC‘s into the muscle

-> Improved muscle function

-> Less fatty infiltration

Oh S, JSES: 2013



BIOLOGIC AUGMENTATION IN CUFF REPAIR: WHERE WE ARE IN 2014?

UNIVERSITÄT BERN

« Shoulder Course »

Day 2

12. Sept. 2014

NOT THERE

BIOLOGIC AUGMENTATION IN CUFF REPAIR: WHERE WE ARE IN 2014?

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Not yet there

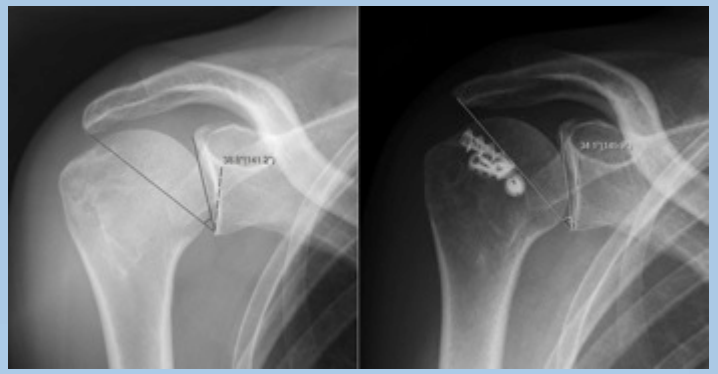
BUT WHERE TO GO?

TAKE HOME MESSAGES: EXTRINSIC

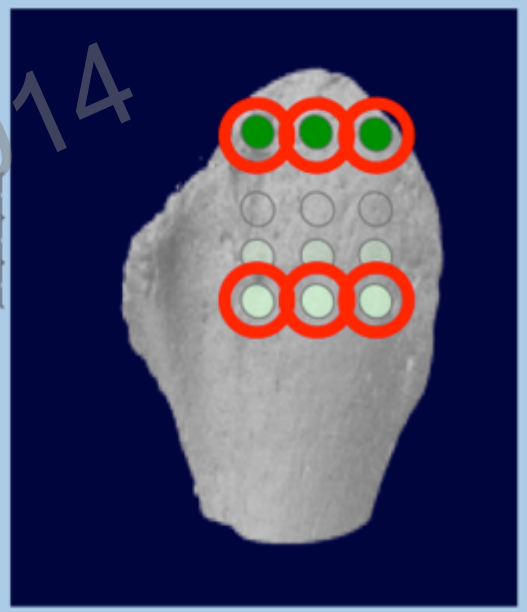
- Age of the patient
- Smoking
- NSAID
- Diabetes mellitus
- Hypercholesterolinemia
- Vit. D deficiency
- Fluoroquinolones

TAKE HOME MESSAGE BONE

- **Critical Shoulder Angle**
  - **— Assessed and reduced**



- **Best anchor position**



TAKE HOME MESSAGE INSERTION + MUSCLE

- **Growth factors (PRP‘s)** x
  - — L-PRP, P-PRP in massive tears √?
- **Progenitor - Stem cells**

  Cell Therapy:
  - — Placenta derived Stem Cells √?
  - — „Simple“ MSC‘s x √?

  Cell Tissue Engineerig:
  - — Transduced stem cells √?

FUTURE

- **Understand the early and late pathological process of...**
  - — **Tendon: Apoptosis, inflammation & degradation**
  - — **Muscle: Atrophy, inflammation & fatty infiltration**

- **VISION: Interfere in this pathways using pharmacological products**

THANK YOU FOR YOUR ATTENTION!

UNIVERSITÄT BERN

Matthias A Zumstein, MD
Shoulder, Elbow & Orthopaedic Sports Medicine
Department of Orthopedic Surgery and Traumatology
University of Berne, Switzerland