Can ultrasound be used for monitoring of exercise effects in tendons, aiming at injury-prevention & guided-rehabilitation?

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Ladies and gentlemen, my presentation is about exercise effects in tendons and the possibilities to monitor these effects with ultrasound. It is also about a new technique called UTC Imaging and it’s benefits for injury-prevention.
Why monitoring of exercise effects?

- Tendon failure preceded by matrix degradation (Webbon 1977, Birch 1998, Thorpe 2010)

However,

- Conventional US can't detect early changes and isn't able to predict SDFT injury! (Gillis 1993, Birch 1999, Avella 2009)
  - US is poorly reproducible
  - Limited increase CSA
  - Grayscale not representative for stage of integrity

Why should we try to detect exercise effects?
Well, there is growing evidence that tendon injuries are frequently preceded by matrix degradation, initially without clinical symptoms. But, several research groups came to the conclusion that it is impossible to detect matrix changes nor predict tendon injuries by means of conventional ultrasonography.
During fundamental research we matched ultrasonographic images exactly with post-mortem macro- and microscopy. To the left a completely normal SDF tendon and to the right a tendon with a huge scar. Despite of the fact that the scar contains no normal structure at all, lots of echoes can still be found in the ultrasonographic image. So, a mesh without structure can barely be discriminated from normal integrity in grayscale images.
limited axial resolution:
\[ \geq 0.38 \text{ mm} \ (10 \text{ MHz}), \geq 0.45 \text{ mm} \ (7.5 \text{ MHz}) \]

\[ \Rightarrow \text{US image is mixture of reflections \& interfering echoes!} \]

Not every Echo does represent Structure!

Why is a grayscale image not discriminative for the stage of integrity.
To put it simple, please compare a tendon with this wall of natural stone.
A tennis ball thrown against this wall will only return in a straight line
when he hits a larger stone, what I call a structural reflection.
In case the same ball hits more than just one small and irregular stones,
the ball won´t come back in straight line, but he will break away and most
probably will interfere with other returning balls.
Simply, the same happens in ultrasonography:
Only larger tendon bundles generate reflections while, on the other hand,
smaller entities like fibrils and cells generate interfering echoes.
As such, the ultrasonographic is a mixture of structural reflections and
interfering echoes.
We concluded that 3-dimensional tendon integrity can not be captured in 2-dimensional ultrasonographic images. You may think I am exaggerating, but in my humble opinion ultrasonographic evaluation of tendons has more to do with Art than with Science.

Don’t worry, that is no disaster; you only have to be aware of these fundamental facts.

And, the positive thing is that most clients pay more for Art than for Science!
Therefore UTC

= Ultrasound Tissue Characterisation

✓ standardised collection of US data
✓ visualises and quantifies 3-D tendon integrity
✓ UTC aims at:
  • monitoring exercise effects
  • early detection of matrix degradation
  • targeted therapy
  • guided rehabilitation of tendon lesions

Therefore we designed UTC, which means ultrasound tissue characterization. This technique visualizes and quantifies 3-dimensional tendon integrity. And, in contrast to conventional ultrasonography, UTC is highly reproducible with standardized scanning and analysis.
This is the device for standardized scanning. The transducer is not operated manually but fixed in transverse position in a tracking device, preventing transducer-tilt. The device also contains an acoustic coupling stand-off. The tracking system is motorized for a gradual movement of the transducer. And, during the sweep along the tendon transverse images are captured every 0.2 mm and stored real-time in a high-capacity laptop computer.
By piling-up (and compounding) all successive transverse images, a 3-dimensional data-block is created, representing a tendon section with a length of 12 cm.

The tendon can be visualized tomographically in 3 planes of view and in a 3-dimensional coronal view:

The coronal views are reconstructions that can not be made with conventional ultrasonography.

Please notice that the 3-dimensional coronal image provides an inward view into the lesion and visualizes perfectly the integrity and continuity of fibres and fasciculi.
Even more important than visualization is tissue characterization and quantification of integrity. Based on dynamics of echopatterns, UTC algorithms can discriminate 4 different echo-types, namely
+ type I, generated by intact and aligned fibres and fasciculi, colored green
+ type II, generated by discontinuous or wavy fibres and fasciculi , colored blue
+ type III, related mainly to smaller fibrils, colored red, and
+ type IV, related mainly to amorphous tissue with cells and fluid, colored black.

Please notice that echotypes I and II are generated by reflections from larger structures, while III and IV are interfering echoes from smaller entities with a size below the limits of resolution.
This slide with grayscale and UTC images of exactly the same tendon segment shows the benefits of UTC-processing.

In contrast to the conventional 2-dimensional image, the UTC-processed image is the resultant of multiple images thus providing 3-dimensional information. Only larger fibers and fasciculi that are integer over longer distances will be colored green or blue while smaller and disorganised fibrils and cells will be colored red and black. In this way the lesion can be discriminated.
Quantification of Integrity:
Normal

- echo-type I = 80-90 %
- echo-type II = 10-15 %
- echo-type III + echo-type IV ≤ 5

Integrity can be quantified.
This is an example of normal superficial and deep flexor tendons.
Normal tendons consist of
* 80 till 90 percent echo-type I, and
* 10 till 15 percent type II

Please notice: barely any type III or IV echoes.
Evaluation of Regenerative Therapy

• standardized central-core lesion
• treatment:
  
  PRP: PRP, contra-lateral NaCl 0.9%
  MSC’s: cells, contra-lateral NaCl 0.9%
• UTC: 0, 1, 2, 3, 5, 8, 12, 18, 24 w.
  
  Bosch G et al 2011

This is an example how UTC is used for staging and objective evaluation of regenerative therapies, for instance with platelet-rich plasma and with stem cells.
Standardized lesions were created in the superficial flexor tendons of both front limbs.
Subsequently healing was monitored regularly by means of UTC.
During repair, various stages of integrity can be discriminated and the excellent reproducibility of UTC offers the opportunity to monitor repair processes.

# Till Day 35 the lesion is extending which is a normal phenomenon during early stages of healing.
# At Day 35 the lesion contains already more red than black echoes indicating fibrillogenesis.
# At Day 84 the lesion has filled in with blue and green echoes. This means early bundles that are not yet aligned.
# At Day 126 bundles are more organized, thus less blue and more green echoes.
This schedule was developed for staging of repair.

* during INFLAMMATION and demarcation of the lesion, there are mainly black echoes, thus haematoma and exsudate
* during FIBRILLOGENESIS, there is a decrease of black echoes and an increase of red ones, indicative for the formation of a fibrillar matrix.
* during ORGANIZATION & BUNDLE FORMATION, green and blue echoes do increase. At the same time, red and black echoes decrease sharply, indicating the organisation of fibrils into tendon bundles.
* during the REMODELING stage, a sharp drop of blue echoes can be observed, thus less integer tendon bundles are remodelled into intact and aligned bundles, colored green.
In these experiments, one limb received treatment while the contra-lateral limb was placebo-treated with the same volume sterile saline. And at 24 weeks horses were sacrificed for post-mortem evaluation.
As UTC is both standardized and quantitative it allows the objective evaluation of therapeutic interventions. For instance, the effects of PRP were compared with those of placebo treatment with the same volume of sterile saline injected in lesions in both front-limbs. Intra-vital UTC-monitoring at several time-points during tendon healing offers great benefits compared to single postmortem investigation of experimental animals! First of all, it can save lives! Furthermore, besides evaluation at end-stage UTC-monitoring also provides utmost important information at various stages of repair. These graphs visualize significant differences (marked by asterisk) between PRP and saline injected lesions at several stages of repair (PRP in solid lines, Saline in dotted lines).

In PRP treated tendons
1. from 1 week post-treatment a significant decrease of echotype IV, thus less amorphous tissue with cells and free fluid, exsudate and/or haematoma. This is indicative for an anti-inflammatory effect.
2. from week 1 till 8 a significant increase of echotype III, thus increase of a dense fibrillogenic matrix, indicative for advanced fibro-proliferation.
3. starting from week 8 significant increases of echotype I and II, indicative for advanced organization of fibrils into tendon bundles (fibers and fasciculi).
4. at end-stage a significant increase of echotypes I and a significant decrease of echotype II which means that tendon bundles are becoming more and more integer and aligned in lines of stress. This indicates advanced remodeling.
A collective name for tendon disorders is tendinopathy, a clinical concept independent of pathogenesis. Tendon injuries may be the result of single macrotrauma. But, as said in my introduction, there is growing evidence that tendon lesions are frequently preceded by gradual disintegration going on for months or even longer before injuries become manifest. So, clinical symptoms are frequently only the tip of the iceberg. This degradation is the result of ageing and of molecular inflammation after repetitive overuse. Early stages of disintegration may be still manageable but when it comes to a tendon rupture, cases with underlying degeneration have by far the worst prognosis. So, early detection is of vital importance! This requires a Pro-Active instead of a Re-Active approach.
Please allow me a short excursion to human sports medicine showing you some examples of ProActive approaches for injury-prevention and rehabilitation.

Since 3 years in a group of professional Australian football-players Achilles and patellar tendons are UTC-scanned bi-weekly.
For instance, these are transverse images of an Achilles tendon after heavy competition. No clinical symptoms and on grayscale no abnormalities. However, on the corresponding UTC-processed image a localized spot, mainly blue which is indicative for matrix swelling and remodeling. These changes may be reversible with adjusted exercise, definitely no rest.
Early Detection

AT routine check-up: no clinical symptoms!
⇒ advice: reduce exercise

However, athlete continued high-impact training 2 weeks later:
symptoms & rupture!!!

UTC detects matrix changes before symptoms
⇒ can be used to prevent injuries!!!

But, there is not always a happy end.
For example, this player showed at regular check-up a localized remodeling, seen as a blue spot in the center of the Achilles tendon. Without any clinical symptoms. These changes had not been observed on a previous check-up some weeks earlier and it was decided to prescribe reduced exercise. Despite this advice, the athlete continued high-impact training. And, regretfully for him, he came back 2 weeks later with a fully-developed partial rupture. This was one of those cases that convinced us of the possibilities to predict tendon injury.
Monitoring of Eccentric Exercise

professional athlete
Patellar Tendon check-up
few days slight swelling & tenderness
eccentric exercise + UTC-guidance
=> within weeks: improved integrity!
=> stayed sound during entire season!

UTC is also used for rehabilitation.
Most cases don’t improve with rest but with physical stimulation, in other words guided exercise.
For instance, this is a nice example of patellar tendinopathy.
To the left the scans at 3 levels, from proximal towards distal of the patellar tendon prior to the start of exercise.
And, to the right the scans after only a few weeks UTC-guided exercise, showing already a significant improvement of integrity.
UTC in Equine Sports Medicine

I. exercise-effects in racehorses
   - short-duration ?
   - fully reversible ?

II. long-term monitoring high-performance horses in jumping, dressage, eventing
   - can we detect overstrain, degeneration ?
   - can we predict injury ?

Based on our observations in human sports medicine we started to investigate exercise effects in the horse too, partly in Australia and partly in the Netherlands.

Main research questions were:
First, can we detect changes in racing thoroughbreds immediately after the race and if so, are these changes of short-duration and fully reversible
Second, can we monitor exercise effects in high performance horses, aiming at early detection of overstraining and degeneration.
And, do UTC scans have a prognostic value. In other words, can we discriminate short-duration exercise-effects from more serious changes like overstrain and degeneration.
Tendon quality, going down

Our equine research is based on the concept of Cook and Purdam, that development of tendinopathy is a continuum.

Previous research indicates that tendon quality is determined at young age and after maturation the possibilities to adapt are gone.

Excessive loads may bring a tendon in a reactive phase or lead to overstrain that can either restore or lead to dysrepair and ultimately to degeneration.

And while this continuum advances the window of opportunity to restore with appropriate exercise is closing more and more.
To test this hypothesis we scanned SDF tendons in young mature racehorses, prior to and during the first 4 days post-race. These scans were compared with those from thoroughbreds that trained but did not race. Please notice that also in this training group limited daily changes can be observed but these changes were not significant in contrast to those in the race-group.

Race-effects did frequently normalize within 4 days post-race.
Short-Duration Effects

- less aligned tendon bundles
- increase remodeling
- increase loose fibrillar matrix
- no free fluid!

=> no matrix degradation
=> most probably cellular response:
  - increased cell metabolism
  - production high-molecular GAG’s

(Scott et al 2004, Cook & Purdam 2008)

may be reversible within 4 days!

Race-effects were moderate but significant.
There is
* decrease of aligned fibers and fasciculi
* increased remodeling
* increase of loose fibrillar matrix and,
* no free fluid (not in interfascicular septa).
As said, these race-effects frequently reverse within less than 4 days post-race.
Therefore we believe that there is no damage to the collagenous matrix, but rather an increased cell metabolism, most probably with increased production of larger GAG’s.
Some cases are more serious. This horse had no history of any tendon pathology. After heavy exercise, the superficial flexor is tender, warm, and slightly swollen. Please notice the enormous increase of black, type IV echoes, indicative for free fluid in the interfascicular septa that are clearly visible in the 3-D coronal view. My approach is to reduce exercise, but definitely no rest! And, I keep monitoring weekly, the contra-lateral limb too. UTC parameters should normalize within 4 till 12 weeks. If not, this tendon has entered the tendinosis cycle leading to persistent degeneration.
This slide shows what can happen in a high performance horse within one single season.

At the start of the season the horse showed no clinical symptoms but on UTC already a mild, yet significant increase of blue type II and red type III echoes can be observed. This tendon is in a reactive phase which is normally reversible but not in this horse.

Eight weeks later: a striking increase of blue type II, red type III and black type IV echoes. This means that the tendon matrix becomes degenerative. However, still no clinical symptoms and the rider continues competition.

Another six weeks later, after a major event, a dramatic rupture. Game over!

This example shows you that UTC can discriminate the degenerative pathway that may lead to rupture long before clinical symptoms.
UTC-CheckUp’s for:
✓ early detection of developing lesions
✓ guided rehabilitation

Based on previous observations, we designed a program for regular check-up’s of high-performance horses.
The check-up program for high-performance horses consists of:
# determining the individual base-line at 3 time-points
# a check-up prior to a major event
# another check at 4-7 days after the event
In case echo-types have normalised we re-scan at 8 till 12 weeks.
In case still abnormal, we scale down exercise and re-scan at 4 weeks.
So, exercise effects can be monitored indeed!
And for those who are prepared to think ProActive instead of ReActive, UTC may facilitate the design of exercise programs to prevent or rehabilitate tendon injuries.
portable
standardized & highly reproducible
3-D visualisation & tissue characterisation
early detection overstraining & degeneration
precise diagnosis & prognostication
targeted & minimally-invasive treatments
objective evaluation & monitoring of therapy
guided rehabilitation

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Thank you for your attention!