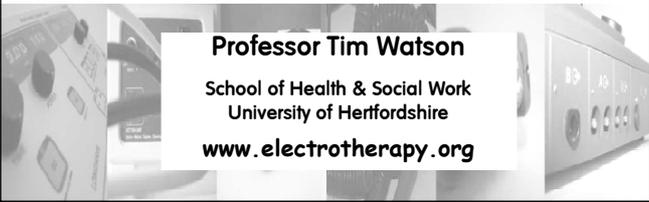




ELECTRO PHYSICAL AGENTS AND TISSUE REPAIR : CAN WE REALLY MAKE A DIFFERENCE?

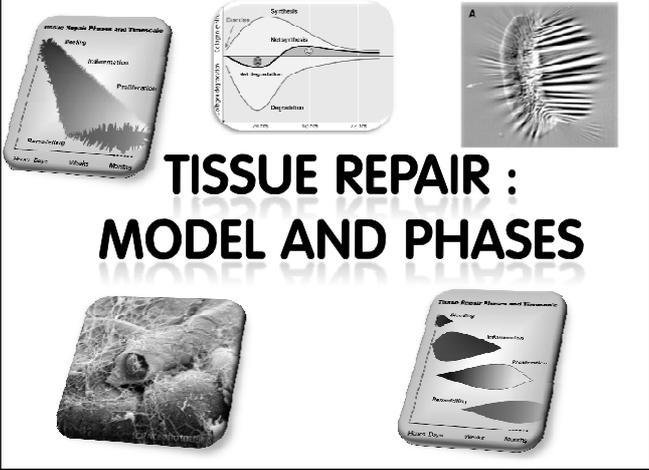
THE OLIVE SANDS MEMORIAL LECTURE 2015

Professor Tim Watson
 School of Health & Social Work
 University of Hertfordshire
www.electrotherapy.org

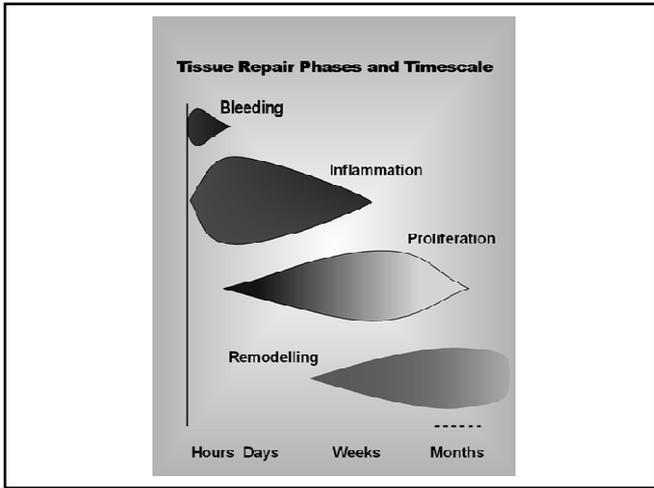


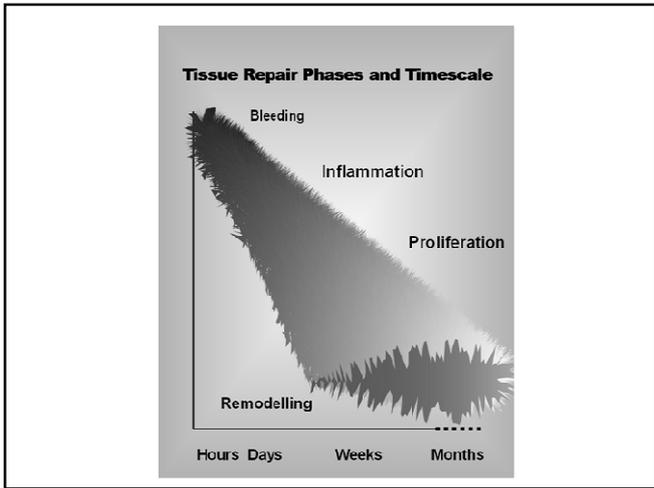
Areas to consider

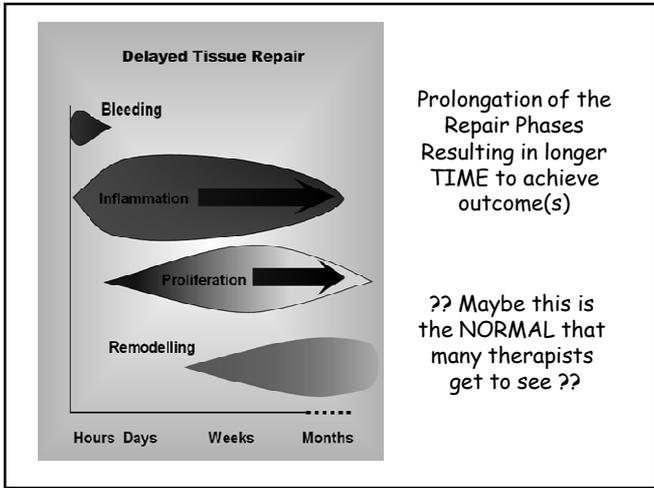
- Basic phasing model of injury and repair
- Electro Physical Agents : Key concepts and Principles
- Influence of EPA's in relation to Tissue Repair
- In passing also consider :
 - Potential mismatch between EVIDENCE and PRACTICE
 - Where might we go in the future?

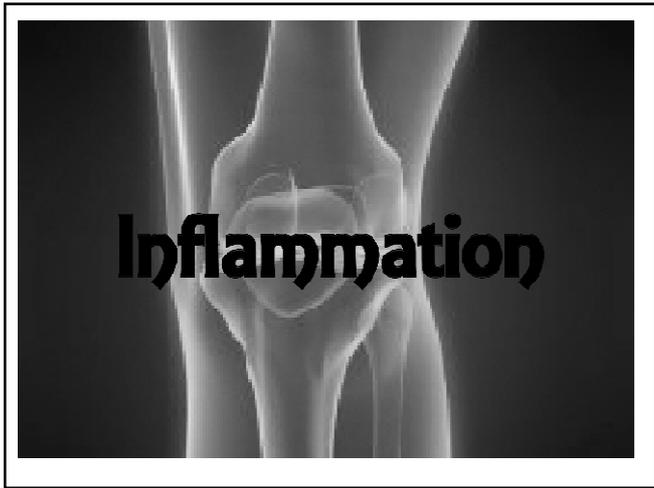


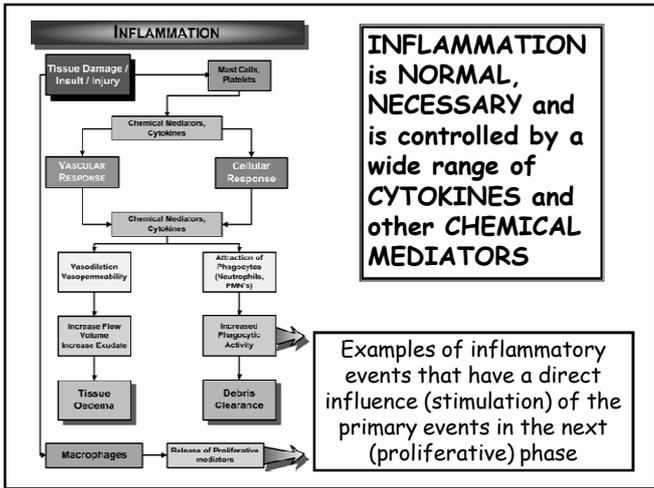
TISSUE REPAIR : MODEL AND PHASES











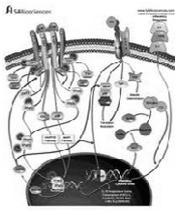
CHEMICAL CONTROL SYSTEMS IN THE INFLAMMATORY PHASE



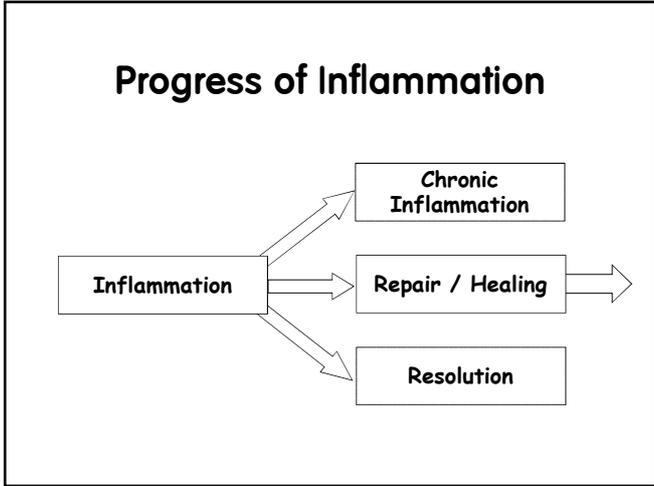
Prostaglandin E2

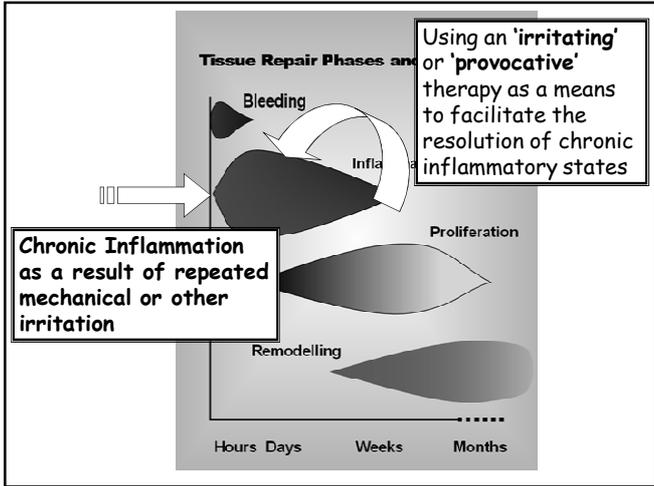


Muscle Fibre Capillary



Inflammatory Cytokine Pathway





Evidence for the presence of chemical 'inflammatory stop' signals

Cellular resolution of inflammation—catabasis

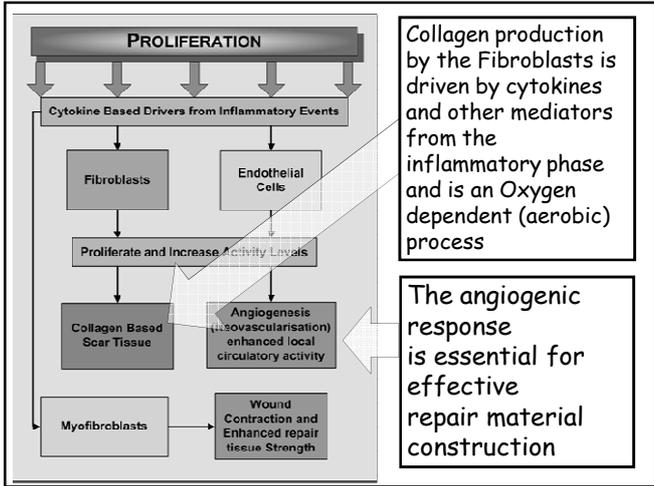
Alan D. Widgerow, MBBCH, MMed (Plast)

catabasis, the resolution of inflammation. These efforts relate to the isolation and understanding of the mechanisms of actions of various "stop signal mediators." These lipoxins, resolvins, and protectins are produced and stimulated by cellular interactions in the blood stream, extracellular matrix, and in cells themselves. Transmission of these signals between cells and the extracellular matrix and between cells themselves occurs via a variety of mechanisms including through intracellular gap junctions, connexins, and cadherins. The existence of these mediators, signals, and channels of communication all provide new therapeutic options for achieving catabasis in a more defined and targeted fashion.

Widgerow (2012)
Cellular resolution of inflammation—catabasis
Wound Repair Regen 20(1): 2-7

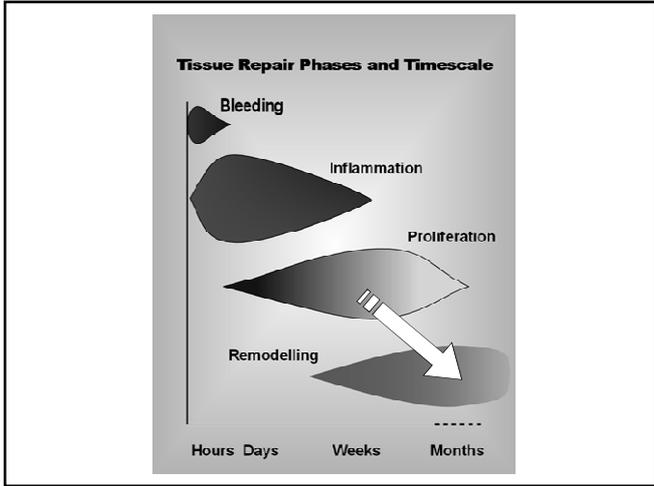


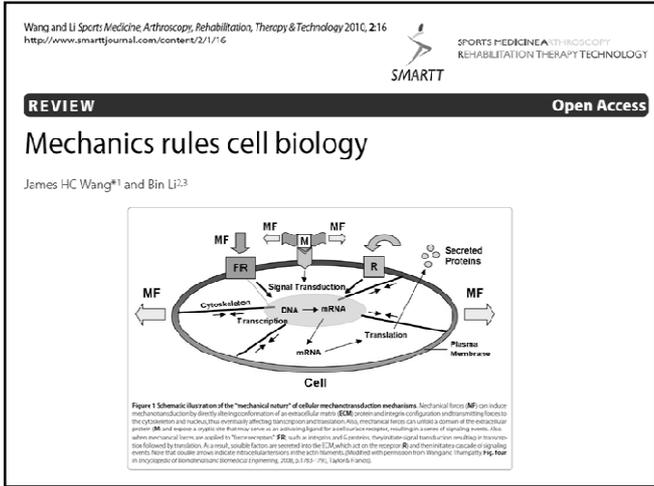
BASIC PROLIFERATION



Factors that STIMULATE and those that INHIBIT angiogenesis in repair (from Li et al, 2005, Adv Skin Wound Care 18(9):491-500)

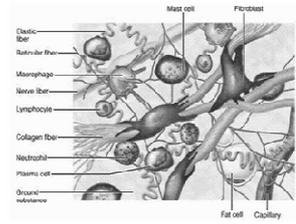
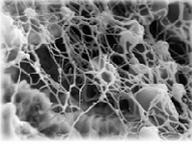
Table 1. ANGIOGENESIS REGULATORY MOLECULES	Table 2. PATIENT FACTORS AND MEDICATIONS KNOWN TO INHIBIT ANGIOGENESIS
Endogenous Stimulators <ul style="list-style-type: none"> - Adrenomedullin - Angiogenin - Angiopoietin-1 - Angiopoietin-related growth factor - Brain-derived neurotrophic factor - Corticotropin-releasing hormone - Cyrils - Erythropoietin - Fibroblast growth factors - Follistatin - Granulocyte colony stimulating factor - Hepatocyte growth factor - Interleukins (IL-3, IL-8) - Midkine - Nerve growth factor - Neuregulin A - Neurotrophin Y - Placental growth factor - Platelet-derived endothelial cell growth factor - Platelet-derived growth factor - Reticularin - Progranulin - Runt3 - Scavengerin - Substance P - Transforming growth factor-β1 - Transforming growth factor-β2 - Tumor necrosis factor-α1 - Vascular endothelial growth factor - VEGF 	Patient factors <ul style="list-style-type: none"> • Increased age • Hypercholesterolemia • Alcohol use • Diabetes Prescription medications <ul style="list-style-type: none"> • Antibiotics (clarithromycin, doxycycline, tetracycline) • Antihypertensive agents (captopril, enalapril, metoprolol) • Diuretics (bumetanide, furosemide) • Nonsteroidal anti-inflammatory drugs • COX-2 inhibitors (celecoxib) • PPAR-γ agonists (pioglitazone, rosiglitazone) Oncology agents <ul style="list-style-type: none"> • Arifametin¹

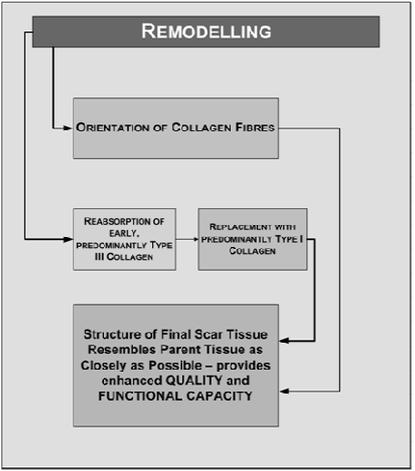


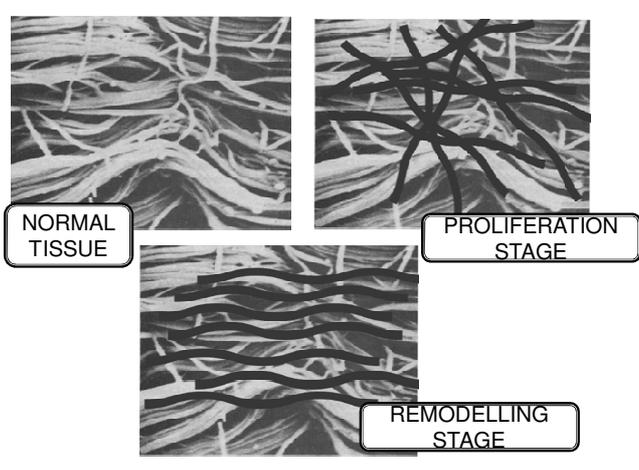


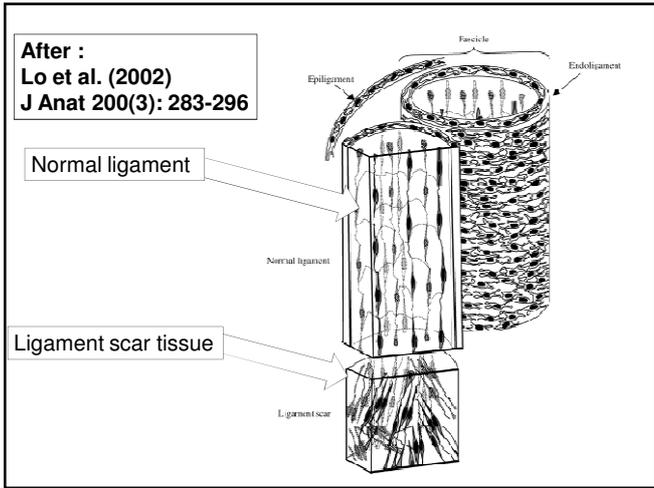
- ### Facilitation of Collagen Synthesis
- Collagen Synthesis is dependent on several key factors :
 - FIBROBLAST presence
 - FIBROBLAST activation
 - OXYGEN
 - NUTRIENTS
 - Important to encourage / enable these elements in order to achieve the most efficient collagen production
 - Tissue OXYGEN DELIVERY appears to be CRITICAL in this regard

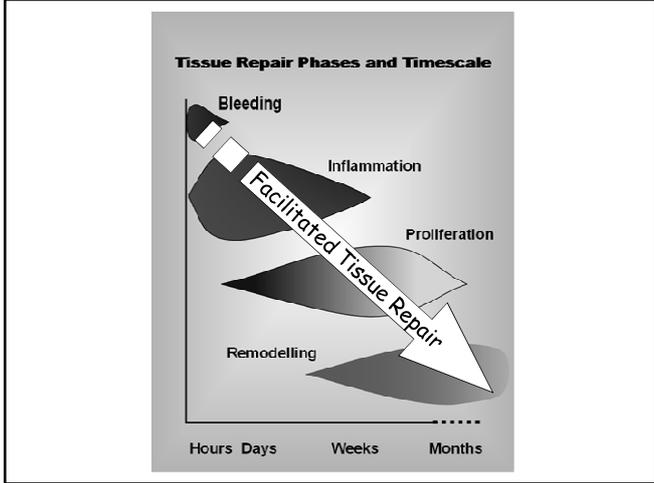
REMODELLING









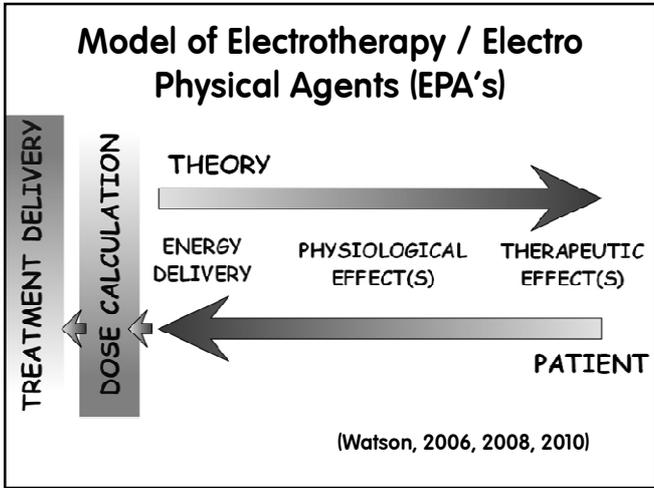


Electrotherapy :: Electro Physical Agents and Repair

What DOES the Evidence say??

Electrical Stimulation Agents / Modalities	Thermal Agents / Modalities	Non Thermal Agents / Modalities
Transcutaneous Electrical Nerve Stimulation (TENS)	Infra Red Irradiation (IRR)	[Pulsed] Ultrasound
Interferential Therapy (IFT)	Shortwave Diathermy (SWD)	Low Intensity Pulsed Ultrasound (LIPUS)
Neuromuscular Electrical Stimulation (NMES)	Microwave Diathermy (MWD)	[Pulsed] Shortwave Therapy (PSWT)
Functional Electrical Stimulation (FES)	Other RF Therapies	[Pulsed] Laser Therapy (LLLT / LILT)
Faradic Stimulation	Hydrocollator Packs	[Pulsed] Microwave Therapy
Iontophoresis	Wax Therapy	Low Intensity RF Applications
High Voltage Pulsed Galvanic Stimulation (HVPGS)	Balneotherapy (inc spa/whirlpool)	Pulsed Electromagnetic Fields (PEMF's)
Low Intensity Direct Current (LIDC) and Pulsed LIDC	Fluidotherapy	Microcurrent Therapies
Twin Peak Monophasic Stimulation	Therapeutic Ultrasound	MAGNETIC THERAPIES
Diadynamic Therapy	Laser Therapy	Pulsed Magnetic Therapy
H Wave Therapy ; Action Potential System (APS)		Static Magnetic Therapy
Russian Stimulation : Medium Frequency Stimulation	Cryotherapy / Cold Therapy / Ice / Immersion Therapy	Microcurrent Therapy (MCT)
Rebox Therapy; Scenar Therapy, NRN (InterX) based therapy		(Radial) Shockwave Therapy
Microcurrent Therapy (MCT)		

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Evidenced EPA's that can (directly) influence Tissue Repair

ESTABLISHED (THE 'CLASSICS')

- Ultrasound Therapy
- Pulsed Shortwave Therapy
- Laser Therapy

EMERGING (EVIDENCED BUT LESS 'POPULAR' IN PRACTICE)

- LIPUS (Low Intensity Pulsed Ultrasound)
- Microcurrent Therapy
- Shockwave Therapy

ALSO

- Magnetic Therapy [incomplete clinical evidence]
- Pulsed Microwave [evidenced but not used]

INDIRECTLY

IFT, TENS, NMES, Russian, Twin Peak Monophasic . . .

Dose – Response Relationship

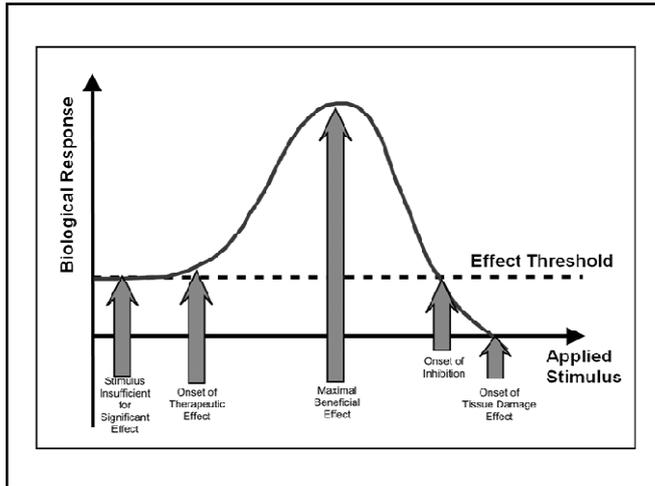
- There is a **SUBSTANTIAL** volume of published research
- More in relation to EPA's than for many other areas of therapy
- **NOT** all supportive – by a long way
- **BUT** the evidence strongly suggests that it is essential to select the optimal **MODALITY** and the optimal **'DOSE'** for optimal effect
- **NOT** really a surprise – same as all other interventions

EPA DOSE WINDOWS CONSIDERED

Key concepts with electrophysical agents

Tim Watson

**Physical Therapy Reviews (2010)
15(4): 351-359**



Problem with 'hitting the wrong window'

- More ways of getting the dose 'wrong' than 'right'
- If you deliver the 'right' therapy and the 'wrong' dose not likely to be optimally effective
- Whether drug based therapy, exercise, manual therapy, acupuncture or any of the electro physical agents
- Plenty of examples in the published literature (reviewed in Watson, 2010)

Examples of Hitting and Missing the Window

**Same Modality (Ultrasound)
Same body area (Shoulder)**

Ultrasound : Dose Issues

- Ainsworth et al (2007) Rheumatology 46(5) 815-20
- Ultrasound and manual therapy for shoulder problems
- Multicentered RCT, double blind and placebo controlled
- Manual therapy + verum ultrasound
- OR manual therapy + placebo ultrasound
- Conclude that the addition of US to the manual therapy made no difference to the outcome
- BUT read the detail

Ainsworth et al (2007)

- US 'dose' determined by treating therapist ('pragmatic' paradigm)
- 80% of the US treatments actually employed US (not 100% as you might expect)
- Dose info only available for 76% of them
- Power ranged from 0.2 – 1.0 W cm⁻²
- Strongest dose was therefore 5 x 'stronger' than weakest
- Treatment times varied by 230% (shortest to longest)
- Whole range of pulse regimes
- Treatment dose 'differential' of at least 1100% weakest to strongest (TW calculated)

Ainsworth et al (2007)

- Given that almost 25% of the ultrasound treatments had no dose recorded
- Given that 20% of people allocated to the ultrasound group did not actually get ultrasound
- Given that the applied doses varied by 100's of percent (actually >1000%)
- Difficult to draw the same conclusion as the authors
- NOT saying that they are INCORRECT, just that it is difficult to 'trust' the findings

Yildirim et al (2013)
 Comparison of ultrasound therapy of various durations in the treatment of subacromial impingement syndrome
 J Phys Ther Sci 25(9): 1151-54.

- RCT to compare the efficacy of ultrasound treatments of various durations for patients with subacromial impingement syndrome
- (US at 1MHz : 1.5 W cm⁻² : Continuous, 5 days/wk : 3 weeks)
- Group 1 (n = 50) : 15 sessions of US @ 4 min
- Group 2 (n = 50) : 15 sessions of US at 8 min
- Both groups get Heat and TENS combined with exercise.
- VAS, UCLA, Constant, and BDI scores showed statistically significant within group improvements.
- When the two groups were compared, we found no statistically significant differences in the Constant activities of daily living, Constant external rotation, Constant force and BDI scores (4/8)
- However, the second group scored better than the first group in all the remaining parameters (4/8)
- **Thus US effective (both groups), but magnitude of the response is dose dependent**

Quick Results and Conclusion

In conclusion, ultrasound therapy was effective at decreasing pain and improving functionality. We showed that 8 minutes of ultrasound administration was more effective than 4 minutes at relieving pain and improving functionality.

4 min US group

→

8 min US group

Table 3. Comparison of the groups after the treatment

	GROUP 1	GROUP-2
VAS*	5.2±1.26	3.38±1.46
Constant pain*	6.20±2.51	8.2±2.57
Constant daily living	13.12±3.21	14.2±4.16
Constant flexion*	7.32±2.00	8.80±3.37
Constant abduction*	6.60±1.62	7.52±1.54
Constant external rotation	8.2±3.39	7.2±2.58
Constant internal rotation*	5.72±2.27	7.0±2.53
Constant force	15.50±12.26	16.38±11.36
Constant total*	59.38±15.32	66.80±19.43
UCLA*	22.70±6.09	29.50±14.85
BDI	12.5±7.68	11.30±8.84

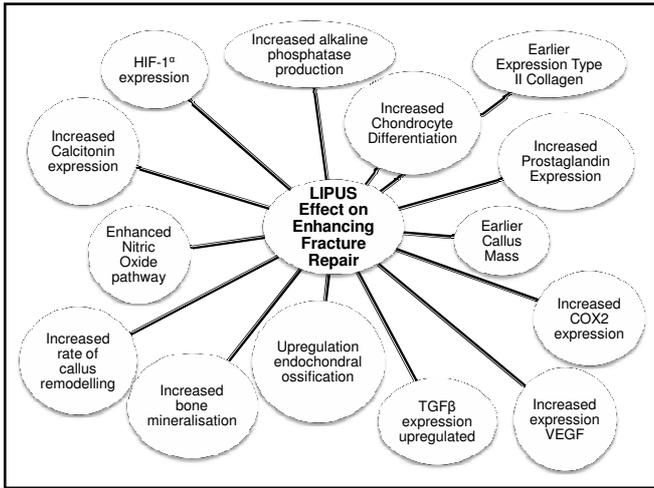
Values are mean ± SD. *p<0.05 from post treatment between two groups
 VAS: Visual Analog Scale; UCLA: University of California at Los Angeles; BDI: Beck Depression Inventory

Both 4 and 8 min US have sig clinical effects BUT 8 min greater effect

Mechanism of Effect

Considerable Commonality

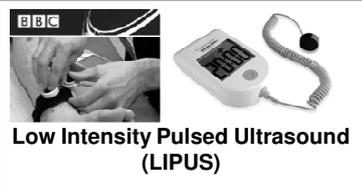
- There is evidence the several EPA's have a significant effect on tissue repair
- There appears to be a commonality in terms of HOW this is achieved
- The CHEMICAL MEDIATOR, CYTOKINE, GROWTH FACTOR enhanced expression, synthesis and release
- Growing body of evidence



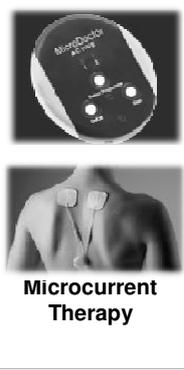
- EVIDENCED, 'CLASSIC' INTERVENTIONS
ULTRASOUND / LASER / PULSED SHORTWAVE**
- Inflammatory optimiser – NOT anti-inflammatory
 - Stimulates / promotes the normal proliferation events
 - Encourages scar tissue remodelling – NOT the 'removal' of excess scar tissue
 - Differential effects in terms of WHICH tissue type
 - Which enables the MODALITY clinical decision

Tissues Absorption Characteristics		
<p>ULTRASOUND Dense Collagen Based Tissues</p> <p>Ligament Tendon Fascia Joint capsule Scar tissue</p>	<p>PULSED SHORTWAVE Ionic, low impedance (WET) tissues:</p> <p>Muscle Nerve Areas with Oedema, Haematoma, Effusion</p>	<p>LASER Superficial Vascular Tissues</p> <p>Open wounds Muscle Nerve Tendon sheath . .</p>

What about the 'non' classical modalities?



Low Intensity Pulsed Ultrasound (LIPUS)



Microcurrent Therapy



Shockwave Therapy

Low Intensity Pulsed Ultrasound (LIPUS)

- Strong evidence (incl RCT) and NICE support
- Established as an effective intervention in the management of BONE injury
- Fresh fracture : Delayed Union : Non-Union
- Reduces the TIME it takes to achieve repair in fresh fractures
- Improves the union rate in delayed and non-unions
- Being investigated for numerous other MSK presentations - ongoing

Shockwave based Therapy

- Different versions – main difference being FOCUSED or RADIAL
- RADIAL (non-destructive) strongest support in therapy arena
- Employed as a PROVOCATIVE stimulus
- Strongest support in CHRONIC TENDINOPATHY
- Also being investigated for numerous other clinical presentations
- Does NOT replace other therapy – used as an ADJUNCTIVE intervention

Microcurrent Therapy

- Been around (different names) for many years
- Strong established effect with BONE and SKIN lesions
- More recent developments with other MSK presentations including muscle, ligament, tendon
- SMALL current delivered over LONG treatment times gaining strongest support

Treatment: NUMBER OF SESSIONS and TREATMENT FREQUENCY is an issue

- Many of the studies employ treatment at frequencies which are not easily delivered in current (practice or NHS) terms, nor realistically the number of sessions
- E.g. Daily ultrasound for 2 weeks : effective but can you deliver it and can the patient afford it?
- BUT there is an increasing availability of HOME BASED Rx – TENS, NMES, Ultrasound, Pulsed Shortwave, Microcurrent



Conclusion I

- Tissue repair sequence is effective and remarkably well organised and controlled
- In therapy, we often get to see the inhibited, slow, delayed or in some other way disturbed repair events – skewed view
- Role of therapy (logic and evidence) is to STIMULATE : PROMOTE : ENHANCE this process – NOT to change it
- Substantial volume of evidence to say this is what we do

Conclusion II

- Electro Physical Agents (EPA's) have an evidenced role in the context of enhancing tissue repair
- Numerous modalities which fulfil this role **ALONGSIDE** other therapy – part of the **PACKAGE**
- **DIFFERENT MODALITIES** achieve optimal influence in **DIFFERENT TISSUES**
- **DOSE** issues are paramount
- Therefore clinical decision making needs to take account of both **MODALITY** and **DOSE**
- If so, the evidence is supportive of a beneficial effect on repair

THANK YOU

www.electrotherapy.org
