THE ROUTINE MAINSTREAM MEDICAL USE OF LLLT WHY HAVE WE NOT ARRIVED YET?

Dr Roberta Chow MB BS (Hons) FRACGP PhD

CLINICAL USE OF LLLT – FOCUS ON PAIN

Disclosure / Credentials

- **GP – Medical Grad 1972 (Hons 2)**
- **FRACGP (1992) – Winner of Monty Kent-Hughes Medal**
- **Other qualifications: Fellowship of the Medical Acupuncture College, Masters Applied Science in Medical Acupuncture, Graduate Certificate of Pain Management (U Syd)**
- **Member Therapeutic Goods Association – Adverse Drug Reactions Advisory Committee, Complementary Medicines Evaluation Committee, Member AMA Council, Examiner with the College of GPs, Member of the Steering Committee for the National Pain Strategy, President of the Australian Medical Laser Association.**
- **Using laser in practice since 1988 – 15mW, 830nm**
- **PhD – 2006 University of Sydney, Faculty of Medicine – Laser treatment of neck pain**
- **National Health and Medical Research Foundation – 3 yr grant to study the effects of laser on nerves**
- **Published 14 papers including a systematic review on neck pain published in the Lancet and four book chapters**
- **Have worked in a large general practice for 25 yrs and now my own practice for 1 yr**

- I have no financial interest or other potential conflict of interest

……why am I doing this??

PREVALANCE & COSTS OF PERSISTENT PAIN

- In the US chronic suffering due to pain costs the country $560 to $635 billion each year in medical bills, lost productivity and missed work.
- 52.5 million Americans are currently living with arthritis, the nation's leading cause of disability and the second most frequently reported chronic condition in the United States.
- Serious, chronic pain affects at least 116 million Americans each year, many of whom are inadequately treated by the health-care system, according to a new report by the Institute of Medicine (IOM).
- By 2030, an estimated 67 million Americans will have arthritis unless the trend is reversed. CDC estimates 8 million new cases of arthritis will be diagnosed in the next decade
- CDC: annual cost of arthritis to the economy was $128 billion in 2003 and increased by $20 billion between 1997 and 2003

Arthritis Foundation

- PERSISTENT PAIN - EPIDEMIC PROPORTIONS

- GLOBAL BURDEN OF DISEASE (2010) – Musculoskeletal disorders make up 21.3% of 777 million disability-adjusted life years (DALYS)

- DALYS for low back pain have increased from 58.2 million in 1990 to 83 million in 2010

- In 25 European countries and beyond 100 million Europeans suffer from musculoskeletal disorders accounting for 49% of workplace absence and 60% of permanent work incapacity in the EU. Cost: €240 billion *Fit for Work? Musculoskeletal Disorders in the European Workforce* Report September 2009

- WHO estimates that 20% of individuals worldwide live with some degree of chronic pain" *The Lancet, Volume 377, Issue 9784, Page 2151, 25 June 2011*

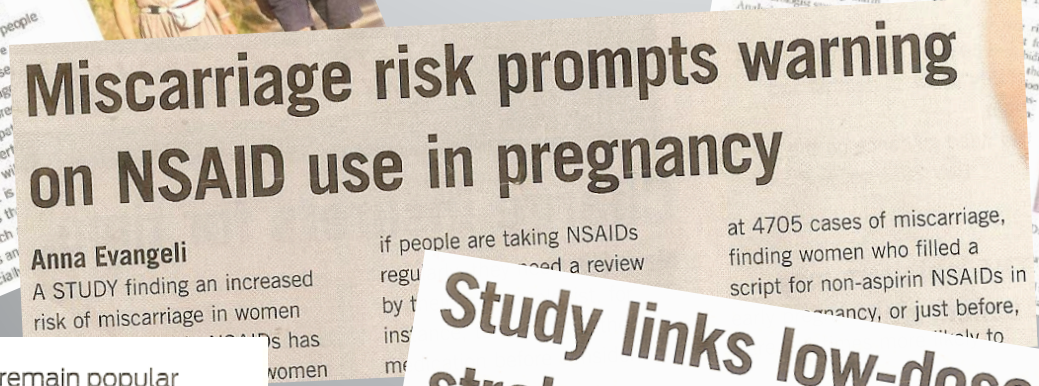
NSAIDS AND SIDE EFFECTS

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used drugs in the world.


COX-2 enzyme inhibitors and heart failure

Q Do cyclooxygenase-2 (COX-2) enzyme inhibitors cause heart failure?

A NSAIDs and COX-2 enzyme inhibitors are not likely to induce a first occurrence of heart failure (HF), but should be avoided in people with pre-existing HF as they are strongly correlated with relapse. A major goal of HF manag... is to identify and reverse pre... factors.[2] The majority of pa... HF have concurrent hypert... blood pressure control w... reduce HF events.[3] It is ... salt-retaining agents th... blood pressure, such ... enzyme inhibitors an... This is especial...


Miscarriage risk prompts warning on NSAID use in pregnancy

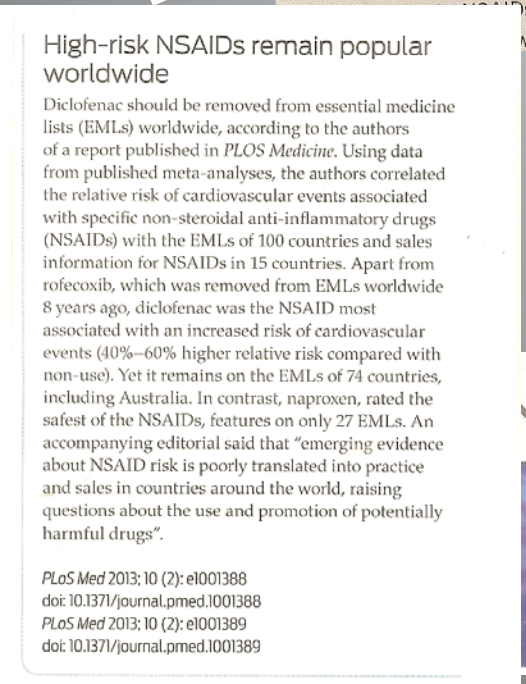
Anna Evangeli

A STUDY finding an increased risk of miscarriage in women ... s has ... women ... if people are taking NSAIDs ... ed a review ... at 4705 cases of miscarriage, finding women who filled a script for non-aspirin NSAIDs in ... gnancy, or just before, ...


NSAID use in aged leads to higher stroke risk

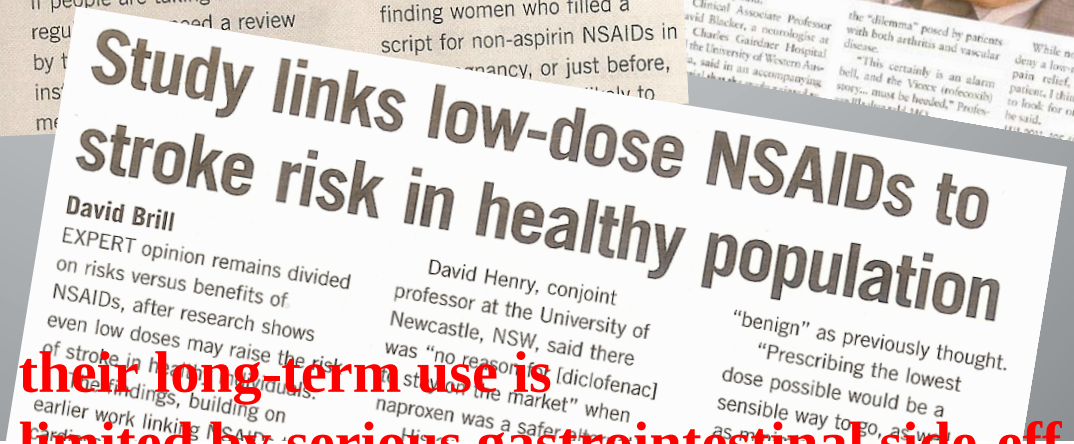
Danny Rose

A STUDY finding that NSAID use is associated with an increased absolute risk of stroke in older Australians should ring alarm bells, a neurologist ... or haemorrhagic stroke following NSAID dispensing equated to an increased absolute risk of 13.4 strokes per ... risk ... for ... Sidn... the ... Dr Caughey said. Clinical Associate Professor David Blacket, a neurologist at Charles Gairdner Hospital ... the University of Western Aus... said in an accompanying ... the "dilemma" posed by patients with both arthritis and vascular disease. "This certainly is an alarm bell, and the Vioxx (rofecoxib) story... must be heeded," Profes... While no-one would want to deny a low-risk patient valuable pain relief, "for a high-risk patient, I think we perhaps need to look for other alternatives", he said.


High-risk NSAIDs remain popular worldwide

Diclofenac should be removed from essential medicine lists (EMLs) worldwide, according to the authors of a report published in *PLOS Medicine*. Using data from published meta-analyses, the authors correlated the relative risk of cardiovascular events associated with specific non-steroidal anti-inflammatory drugs (NSAIDs) with the EMLs of 100 countries and sales information for NSAIDs in 15 countries. Apart from rofecoxib, which was removed from EMLs worldwide 8 years ago, diclofenac was the NSAID most associated with an increased risk of cardiovascular events (40%–60% higher relative risk compared with non-use). Yet it remains on the EMLs of 74 countries, including Australia. In contrast, naproxen, rated the safest of the NSAIDs, features on only 27 EMLs. An accompanying editorial said that "emerging evidence about NSAID risk is poorly translated into practice and sales in countries around the world, raising questions about the use and promotion of potentially harmful drugs".

PLoS Med 2013; 10 (2): e1001388
doi: 10.1371/journal.pmed.1001388
PLoS Med 2013; 10 (2): e1001389
doi: 10.1371/journal.pmed.1001389


Study links low-dose NSAIDs to stroke risk in healthy population

David Brill

EXPERT opinion remains divided on risks versus benefits of NSAIDs, after research shows even low doses may raise the risk ... of stroke in ... findings, building on earlier work linking ... David Henry, conjoint professor at the University of Newcastle, NSW, said there was "no reason ... [diclofenac] ... the market" when naproxen was a safer ... "benign" as previously thought. "Prescribing the lowest dose possible would be a sensible way to go, as ...

their long-term use is limited by serious gastrointestinal side-eff ects.


NSAIDs: study suggests no safe dose post-MI

NYSSA SKILTON

THERE is no safe dose of anti-inflammatories for people with a history of myocardial infarction, research finds, reigniting debate on the risks of over-the-counter NSAIDs.

The Danish study of almost 85,000 patients with prior MI found both short- and long-term use of NSAIDs increased the risk of a further MI and death.

Those taking any NSAIDs over the eight-year study period faced a 45% increased risk of death or MI at the beginning of treatment, and this risk persisted throughout the treatment duration.

The authors called for limits on NSAID use, noting the increase in risk with diclofenac (Voltaren) was higher than for rofecoxib (Vioxx), which was withdrawn in 2004.

"The present results indicate that there is no apparent safe therapeutic window for NSAIDs in patients with prior MI," they wrote in *Circulation*.

Professor Len Kritharides, head of cardiology at Concord Hospital in Sydney, said the study added to mounting evidence that NSAIDs increased cardiovascular risk, but said he did not support an outright ban for CVD patients.

"The advice would be to avoid the drugs where possible, to take them for the shortest period of time possible and to take them under supervision of a family doctor," he said.

"The most important thing is that there's a warning to patients ... and ideally, that patient information, verbal and written, [acknowledges] this risk so that patients know what they're doing."

The study adds to growing evidence

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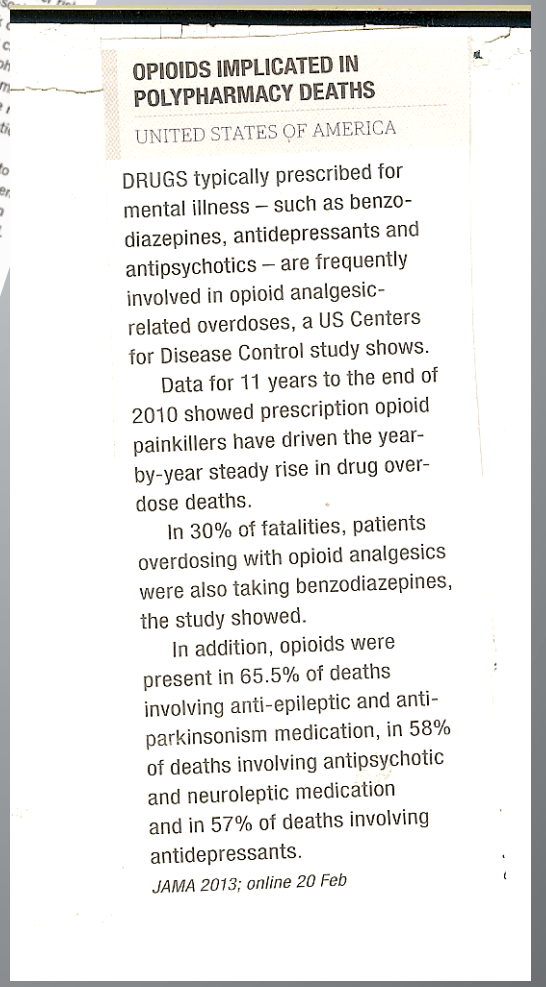
Opioids



OPIOIDS IMPLICATED IN POLYPHARMACY DEATHS

UNITED STATES OF AMERICA

DRUGS typically prescribed for mental illness – such as benzodiazepines, antidepressants and antipsychotics – are frequently involved in opioid analgesic-related overdoses, a US Centers for Disease Control study shows.

Data for 11 years to the end of 2010 showed prescription opioid painkillers have driven the year-by-year steady rise in drug overdose deaths.

In 30% of fatalities, patients overdosing with opioid analgesics were also taking benzodiazepines, the study showed.

In addition, opioids were present in 65.5% of deaths involving anti-epileptic and anti-parkinsonism medication, in 58% of deaths involving antipsychotic and neuroleptic medication and in 57% of deaths involving antidepressants.

JAMA 2013; online 20 Feb

Opioids may promote tumours

Lynnette Hoffman

OPIOIDS given to reduce pain in cancer patients may actually promote tumour growth and metastasis, two studies suggest.

In one study, based at the University of Chicago, overexpression of opioid receptors in a lung cancer cell line increased *in vitro* and *in vivo* measures of tumour growth and metastasis.

In another study, based at the University of North Carolina at Chapel Hill, naturally occurring genetic differences in opioid receptor biology correlated to breast cancer survival in a cohort of more than 2000 women.

Breast cancer mortality was significantly reduced (at least halved) in patients with a genetic variant in the opioid receptor that reduces opioid response.

Several studies have shown a reduced incidence of cancer recurrence after reduced doses of opioids post-surgery for breast, prostate and colon cancer and melanoma, although others have not detected any significant differences, the authors of the lung cancer study noted.

They said their results implicated opioids in these epidemiological findings.

But Melbourne Health anaesthetist Dr Malcolm Hogg, president elect of the Australian Pain Society, called that "a big jump".

He said that while it was important to be aware of the link, other factors likely contributed to the outcomes.

"Whilst opioids themselves appear to inhibit immune cell function in the laboratory, we also know that poorly controlled pain impairs immune function," Dr Hogg said. "So removing opioids and having poorly controlled pain could potentially be just as detrimental.

"When you've got less pain, you've got less stress reaction, and so we believe the immune system functions better."

He said patients should be given a combination of simple analgesics such as paracetamol and anti-inflammatories – along with nerve-modulating medication to improve pain control.

"This can have the effect of limiting reliance and dosage levels of opioids, but opioids should not be excluded."

Anesthesiology 2012; 116:857-67;896-902

Opioid epidemic in the United States.

Manchikanti L et al Pain Physician. 2012

- One in 6 or 17.3% of users of non-therapeutic opioids indicated that they received the drugs through a prescription from one doctor.

- The escalating use of therapeutic opioids shows hydrocodone topping all prescriptions with 136.7 million prescriptions in 2011, with all narcotic analgesics exceeding 238 million prescriptions.

- opioid analgesics are now responsible for more deaths than the number of deaths from both suicide and motor vehicle crashes, or deaths from cocaine and heroin combined.

Physicians for Responsible Opioid Prescribing.

- Despite low-quality evidence supporting practice change, use of chronic opioid therapy (COT) for chronic non-cancer pain increased dramatically over the past two decades.

- Concurrently, opioid analgesic overdose deaths, addiction, misuse and diversion have increased markedly. COT may provide modest, variable short-term pain relief for some patients with chronic pain. Long-term benefits of COT for chronic pain have not been established. Potential medical and behavioral harms of opioids are an important concern…

- Escalating the prescribing of opioids has been repeatedly linked to a myriad of individual and public harms, including overdose deaths. Many patients on long-term opioids may never be able to taper off them, despite their associated toxicities and lack of efficacy.

- Long term opioid therapy may cause adverse effects on the respiratory, gastrointestinal, musculoskeletal, cardiovascular, immune, endocrine and central nervous systems.(Hayes 2013)

- A US healthcare data study of those prescribed opioids continuously over 90 days and then followed up for up to half a decade, showed about two-thirds remained on them.37

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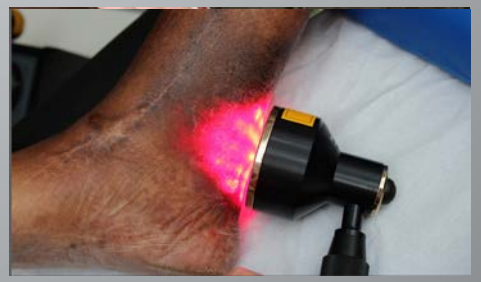
OVERVIEW OF THE USE OF LLLT

Physiological effects of LLLT

- Tissue Repair
- Inflammation
- Oedema
- Analgesia
- Protective (muscle fatigue, oral mucositis)

Applications for LLLT with moderate-strong evidence

- Tendinopathies (Achilles, lateral epicondylitis)
- Chronic joint disorders (OA, RA)
- Back and neck pain (sciatic pain, whiplash)
- Neuropathic pain (PHN, trigeminal neuralgia)
- Non healing wounds (diabetic, venous, pressure)
- Cancer therapy side-effects (Oral Mucositis, lymphoedema, Radiation dermatitis,)
- Dental (post-extraction, TMJ, HSV, orthodontic pain and accelerated tooth movement)

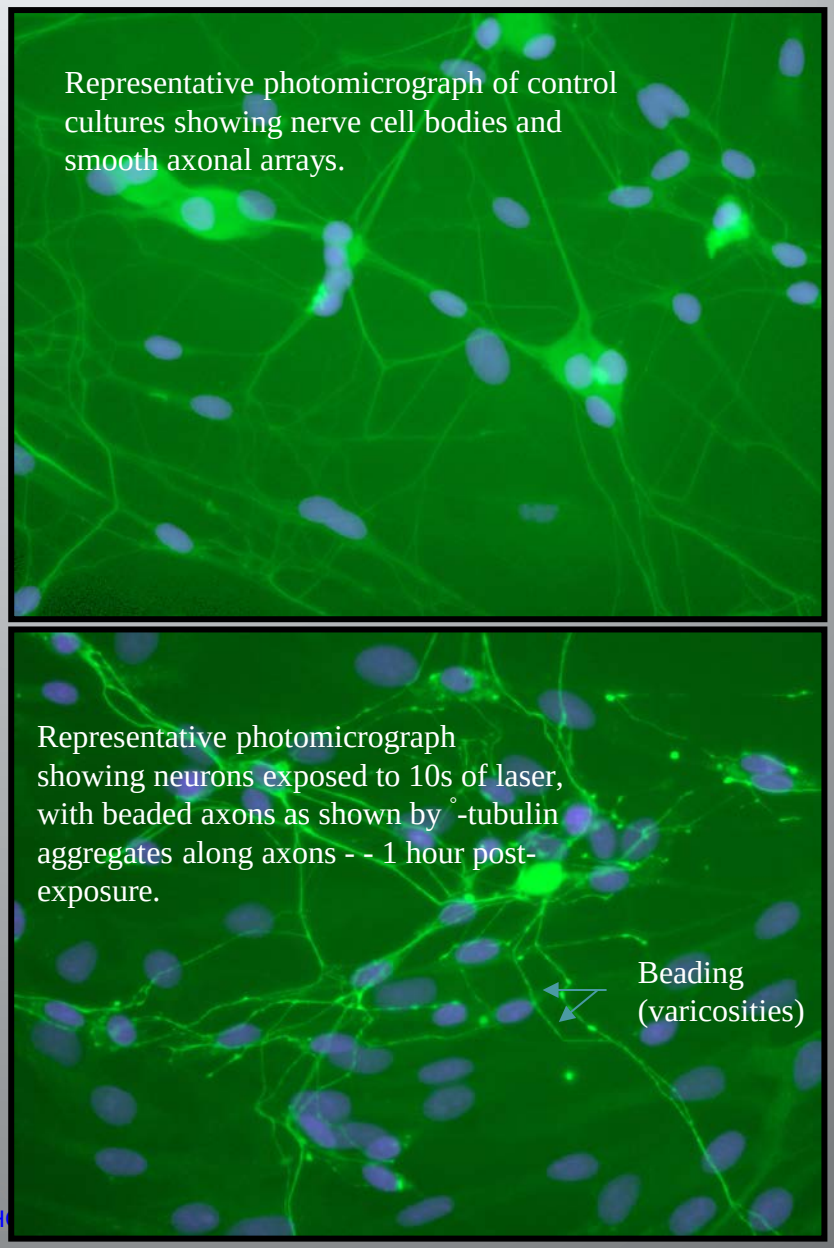


My research

- Most other doctors did not believe in what I was doing…..so I thought I would put it to the test
- I believed in evidence-based medicine
- My observation: some patients reported numbness during treatment – was it a direct effect on nerves?
- Clinically based studies: Review of the literature, a pilot study, an RCT on neck pain
- Lab studies: investigation of effects of laser on nerves

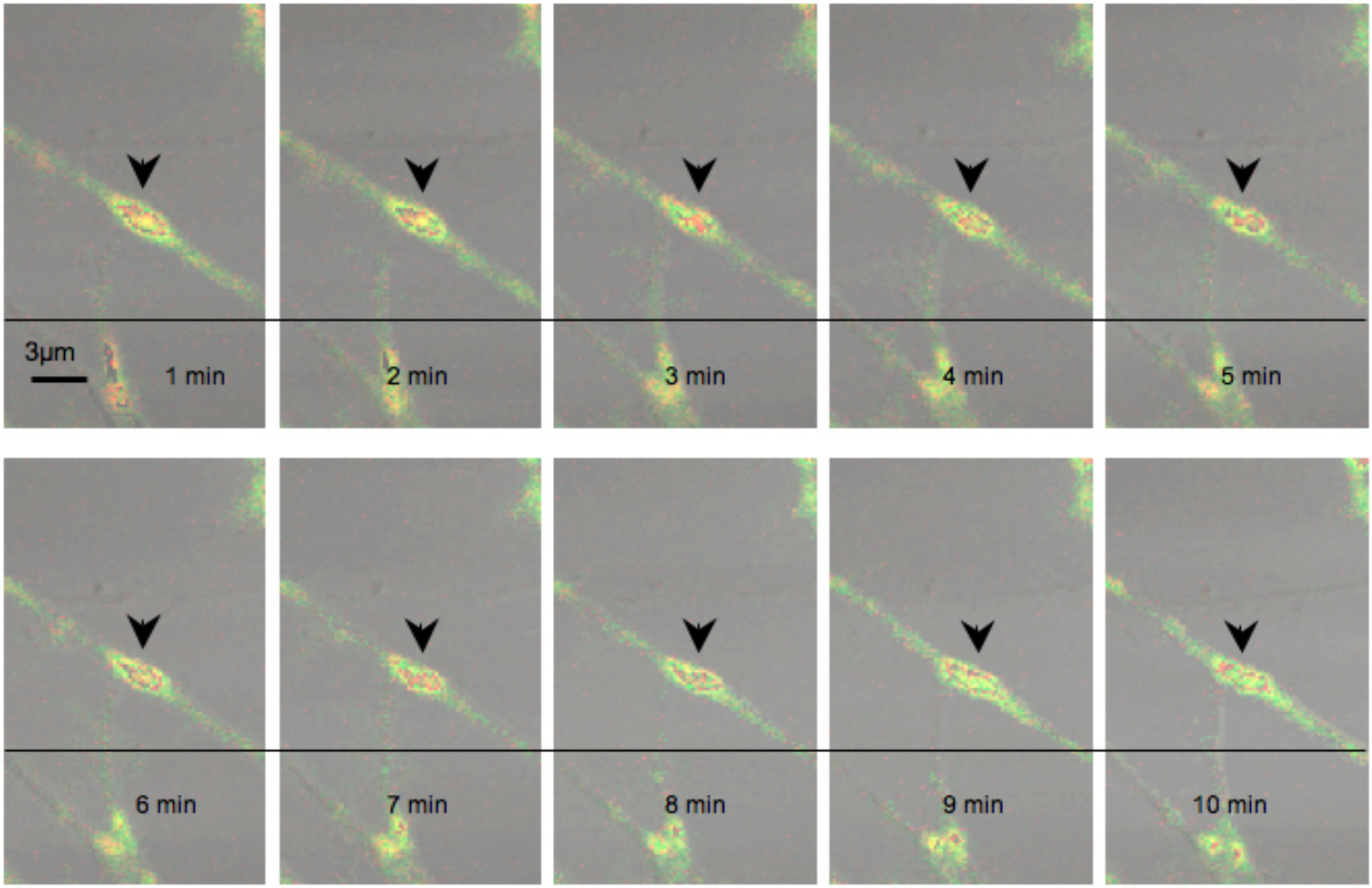
Effects of laser on nerves

- Immunohistochemistry
  - Cultured, neonatal rat dorsal root ganglion neurons
  - Immunohistochemistry - anti-β tubulin antibodies
- Live cell imaging - JC 1
  - Measured Mitochondrial Membrane potential
  - Fast axonal flow
- 650nm, 808nm & 830nm LI

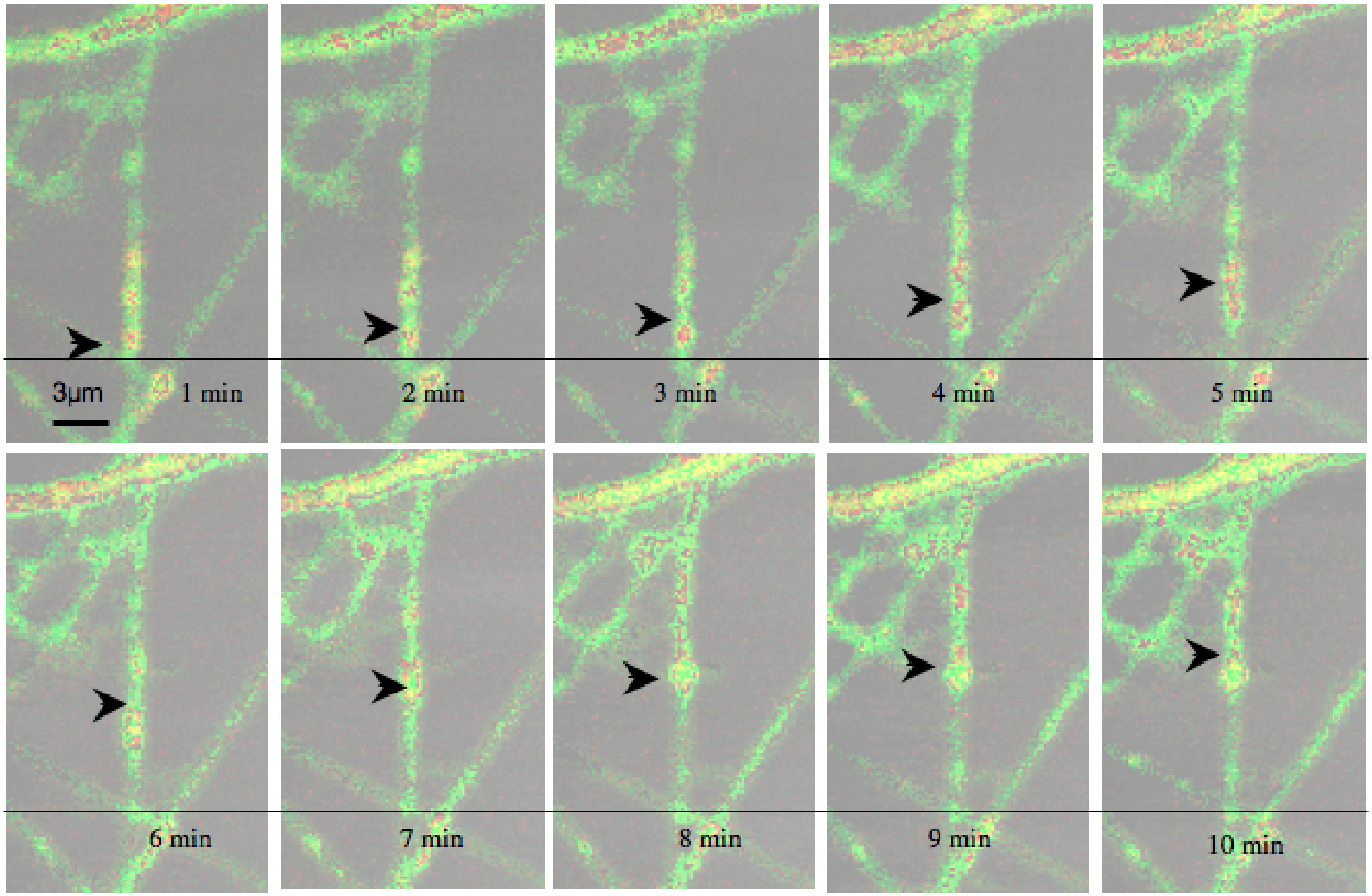


Chow R., David, M., Armati PJ. (2007). J Peripher Nerv Syst 12, 28-39.

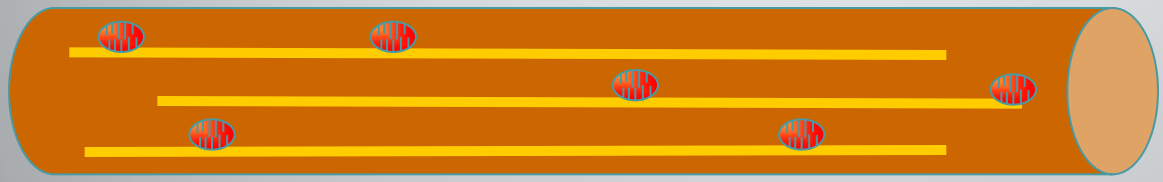
LASER-IRRADIATED AXON SHOWING VARICOSITY IN REAL TIME OVER 10 MINUTES OF OBSERVATION - LI



CONTROL AXON SHOWING NORMAL FAST AXONAL FLOW



FAST AXONAL FLOW- TRANSPORT OF MITOCHONDRIA – LASER DISRUPTS THE CYTOSKELETON



Before LI

AFTER LI

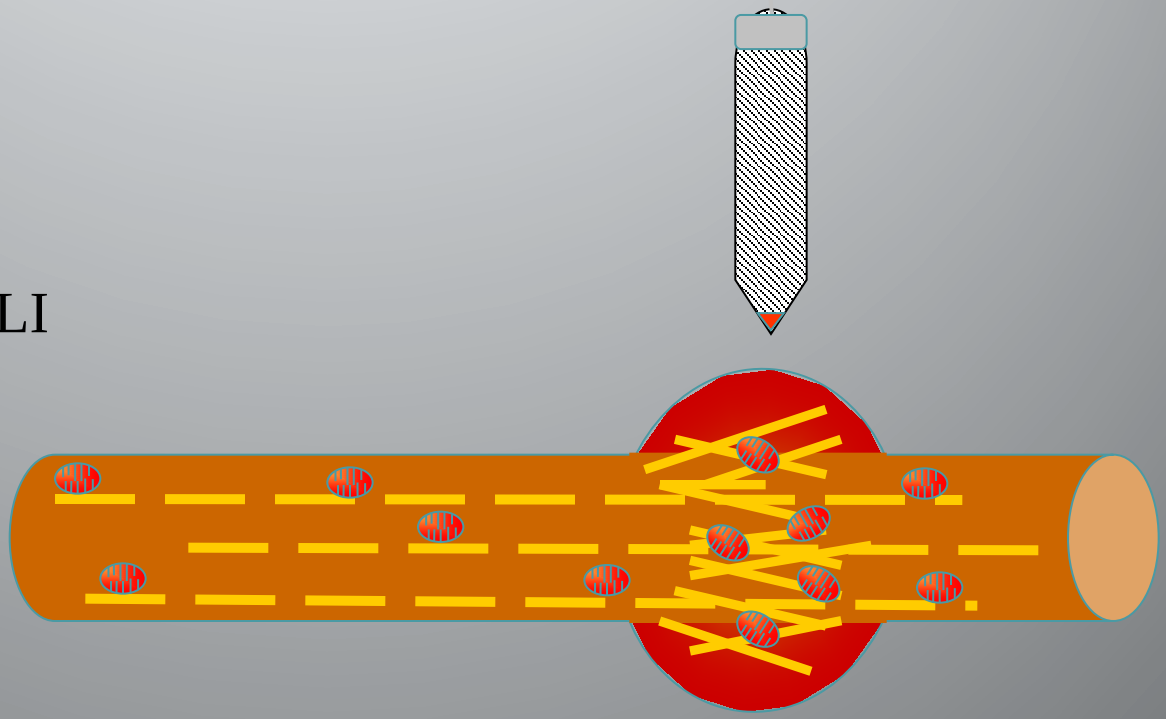


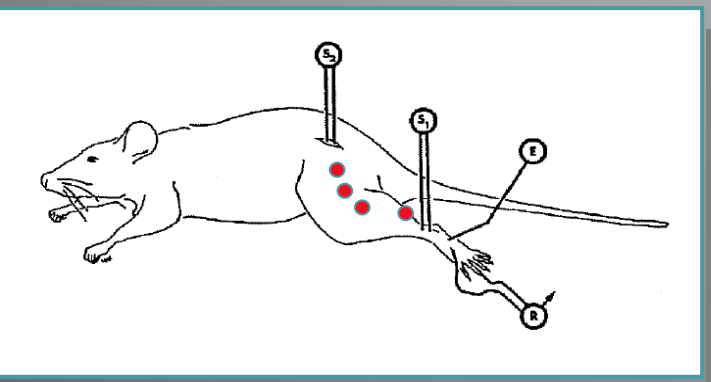
*diagram not to scale

Compound Muscle Action Potential (CMAP)

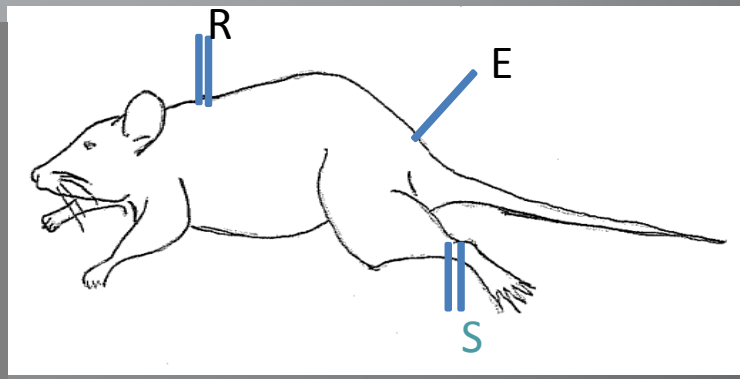
- is the electrical recording of the combined action potential of all muscle fibres
- measures latency of the action potential (time from stimulus to positive n wave) and amplitude (height of the positive wave)
- is a measure of motor nerve function
- reflects conduction velocity

Somatosensory Evoked Potential (SSEP)

- is an electrical recording of the maximal response of sensory nerves at the spinal cord (L1/T12) to supramaximal stimulation of the sensory nerves in the skin at the ankle
- stimulation: in skin at ankle and recording in skin proximally at L1/T12
- is measured orthodromically - i.e. in the direction of normal nerve conduction
- is a measure of function of sensory fibers



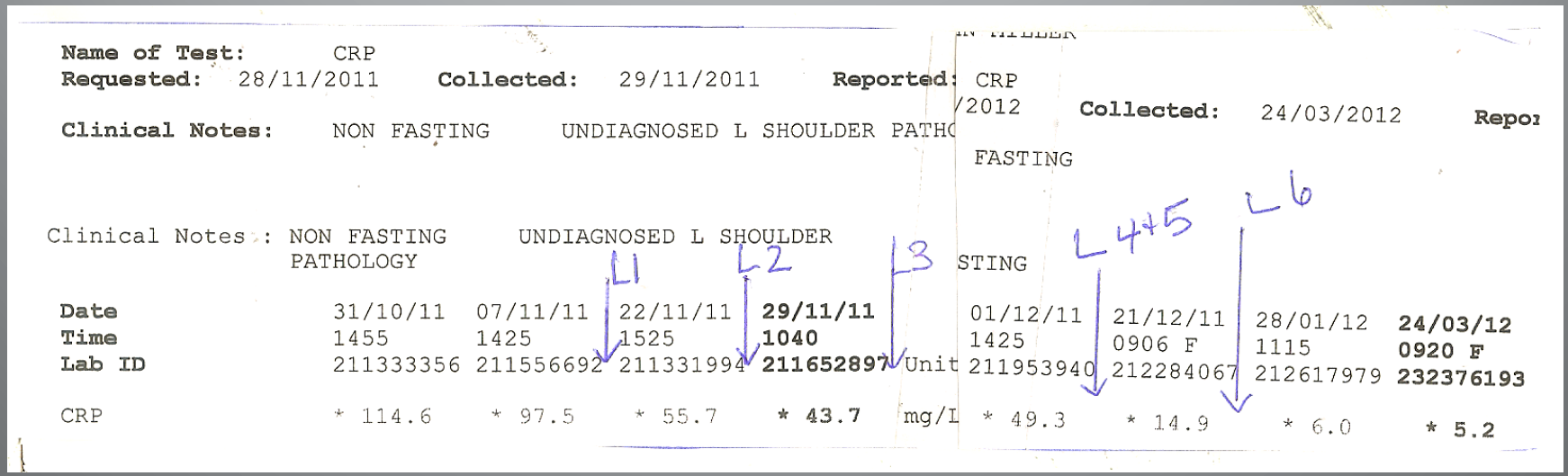
Laser Suppressed nerve conduction in both sensory &motor nerves



- Laser blocks nerves and this has been demonstrated in lots of nerve models
- It is selective for pain fibres
- Once pain fibres are blocked inflammation is also reduced
- The cascade of pain is inhibited

……*but doctors still don't accept it*

- 50yr old female with an extremely painful frozen shoulder for 6 months - to have an arthroscopic biopsy of the shoulder joint lining
- No health insurance
  - Cost $6,000
- Had treatment – no need for biopsy – dx severe frozen shoulder



Name of Test: CRP
Requested: 28/11/2011 **Collected:** 29/11/2011 **Reported:** CRP
/2012 **Collected:** 24/03/2012 **Repo**
Clinical Notes: NON FASTING UNDIAGNOSED L SHOULDER PATH
FASTING

Clinical Notes : NON FASTING UNDIAGNOSED L SHOULDER
PATHOLOGY

L1 L2 L3 L4+5 L6

Date	31/10/11	07/11/11	22/11/11	**29/11/11**		01/12/11	21/12/11	28/01/12	**24/03/12**
Time	1455	1425	1525	**1040**		1425	0906 F	1115	**0920 F**
Lab ID	211333356	211556692	211331994	**211652897**	Unit	211953940	212284067	212617979	**232376193**
CRP	* 114.6	* 97.5	* 55.7	*** 43.7**	mg/L	* 49.3	* 14.9	* 6.0	*** 5.2**

Systematic reviews and guidelines

- BMJ sports medicine journal 2010, frozen shoulder "strong evidence”
- IASP 2010 "strong evidence" myofascial pain syndrome.
- American Physical Therapy Association guidelines for Achilles tendonitis
- The Lancet 2009 acute and chronic neck pain
- WHO 2008 Neck Pain
- MASCC Oral Mucositis

Systematic reviews and guidelines

- Over 400 RCTs
- Over 4,000 laboratory studies
- USA, European, Canadian and Australian regulatory approvals for LLLT
- But no reimbursement by any insurance company or government healthcare system (except Norway)

SO HOW FAR HAVE WE GOT?

YOUR THOUGHTS ON WHY LLLT IS STUCK AND WHAT NEEDS TO BE DONE

Why LLLT is still a fringe therapy and what is missing?

- Mechanism of action?
- Clinical evidence?
- Regulatory approval?
- Reimbursement?
- Key opinion leaders?
- Lack of guidelines?
- Return on investment for doctors and therapists?
- Lack of marketing by manufacturers?
- No industry standard?
- Too good to be true?
- Doctors refuse to believe that light can heal?

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