

***Pain In Cancer Survivors  
Post Breast Cancer Surgical Pain***



**Dr John E. Williams**  
**Consultant in Anaesthesia & Pain Medicine**  
**Royal Marsden Hospital**  
**[john.williams@rmh.nhs.uk](mailto:john.williams@rmh.nhs.uk)**

# What is important?

1. **Real & increasing phenomenon, patients & health care professionals need to be aware**
2. **A form of neuropathic pain**  
**Treatment = neuropathic drugs + physical and psychological therapies**
3. **Acute – to - chronic**  
**preventative strategies important**  
**= a real example of ‘preemptive analgesia’**



# Chronic Pain in the Cancer Survivor: A New Frontier

*A W. Burton, G J. Fanciullo, M, Ralph, D Beasley, M J. Fisch,*

*Pain Medicine 2007:8; 189*

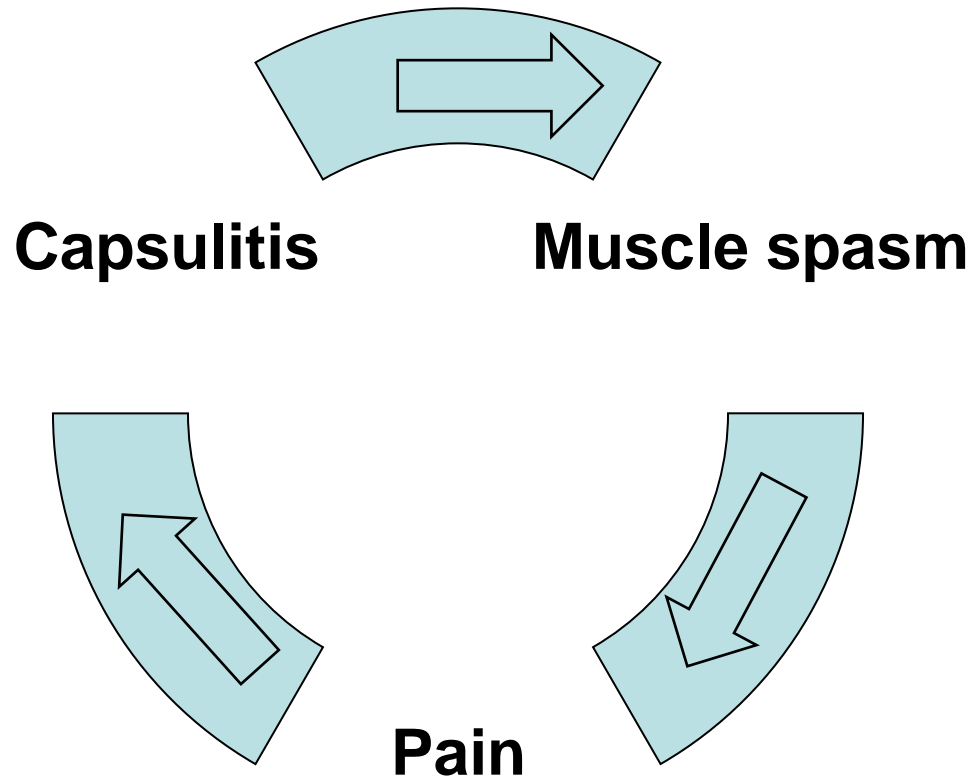
- **Cancer-related death rate has dropped** by 1.1% per year from 1993–2002.
- **2 out of 3 adults will survive cancer**, whereas 50 years ago just 1 out of 4 survived
- The landscape of "cancer pain" is shifting quickly into a **chronic pain situation**, blurring previous lines of distinction in treatment strategies most suited for "chronic" versus "malignant" pain
- Adopting **chronic pain treatment strategies** may lead to optimal outcomes
- As cancer evolves into a **chronic illness**, with co-morbid conditions, recurrent cancer, and treatment toxicities from repeated antineoplastic therapies, pain management challenges in the oncologic patient continue to increase in complexity.

## Case Vignette

- Mrs. MB, age 45
- Mastectomy & axillary dissection, RT, 1997
- Presents with severe chronic pain 1999
- Severe limitation of movement
- MRI excludes recurrent disease

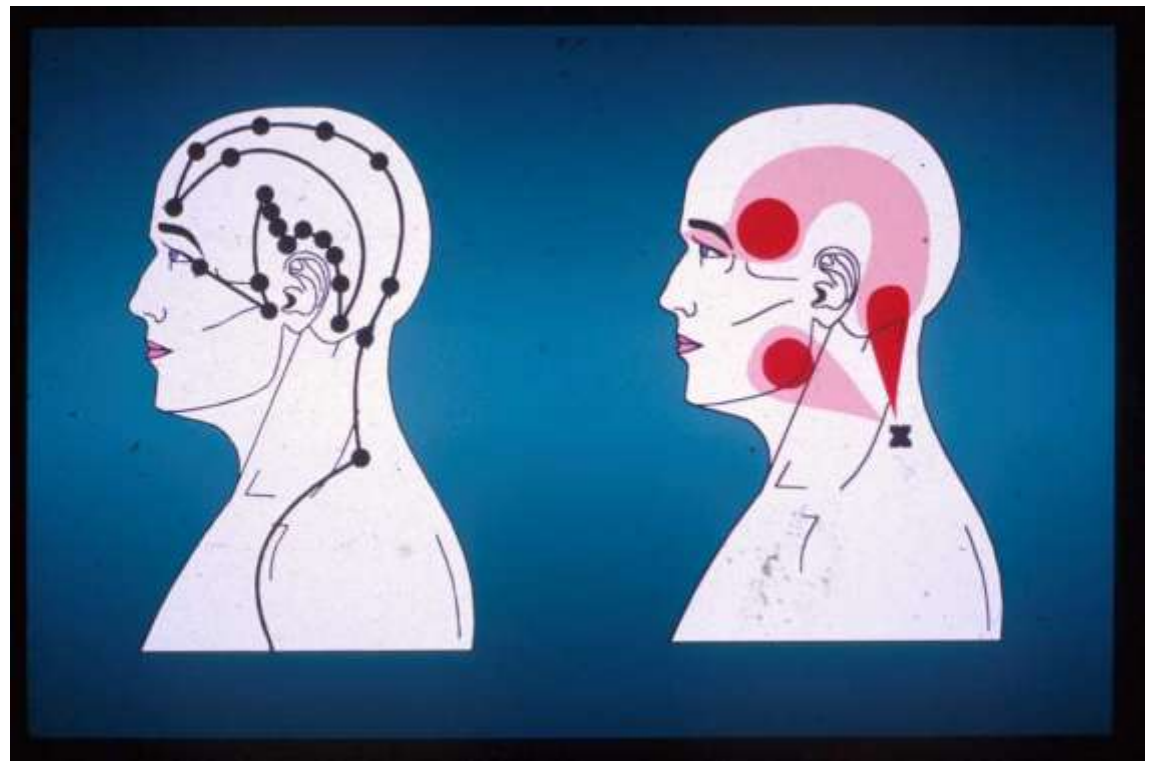
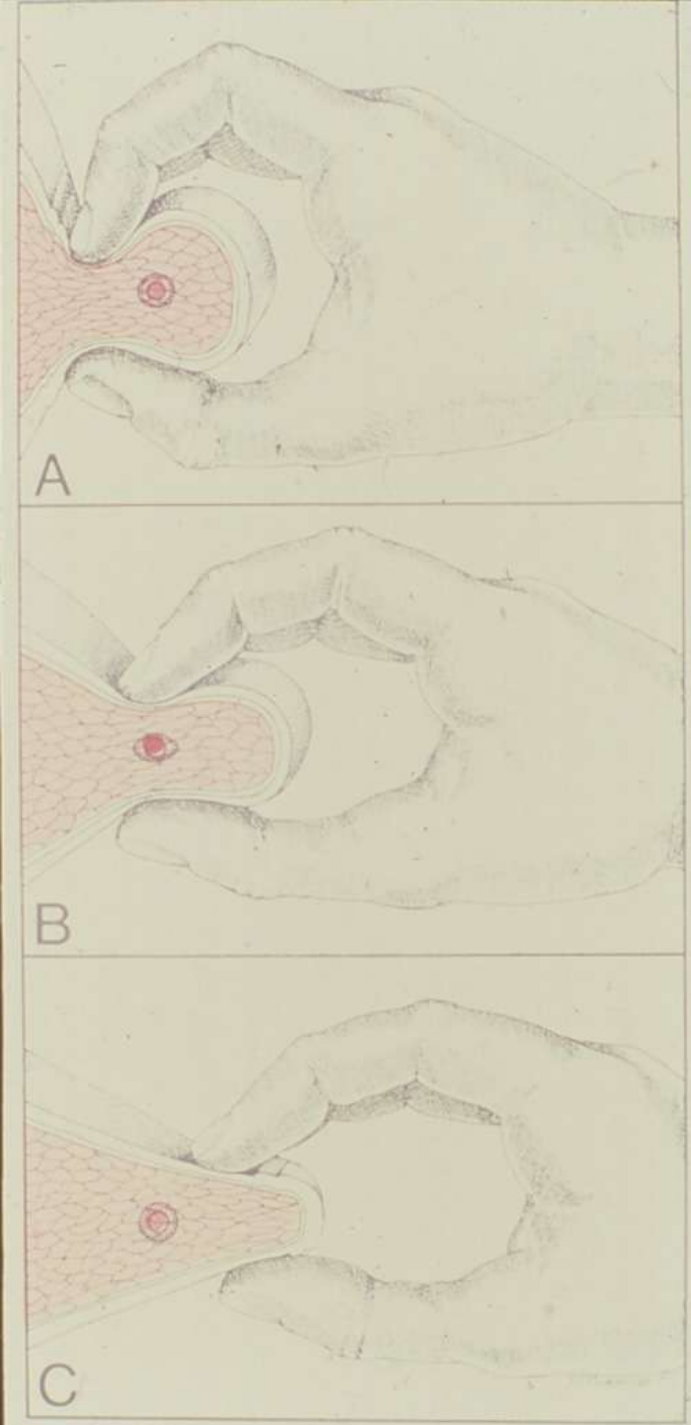


# Pain & disability





***'Cording'***



## 4 patterns of Chronic pain after breast surgery

*Stevens et al 1995*

1. Intermittent, activity dependent, mild 10%
2. As above, mild-moderate, worsening as day progresses, 42%
3. Continuous background pain with mild – severe exacerbations precipitated by activity, 32%
4. As above, worse in morning, reducing as day progresses, with least pain mid morning, progressing again to evening 16%



# Prevalence of chronic pain after breast surgery

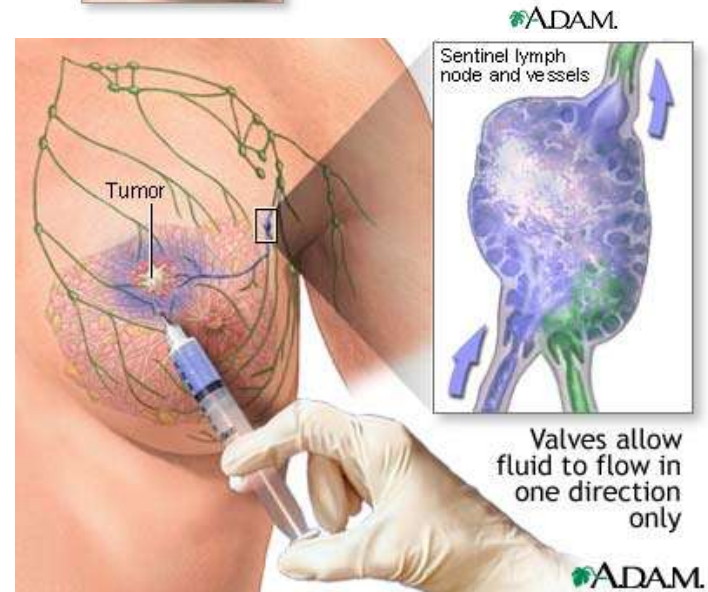
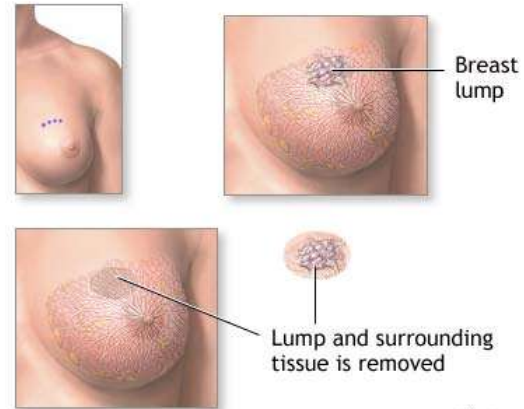
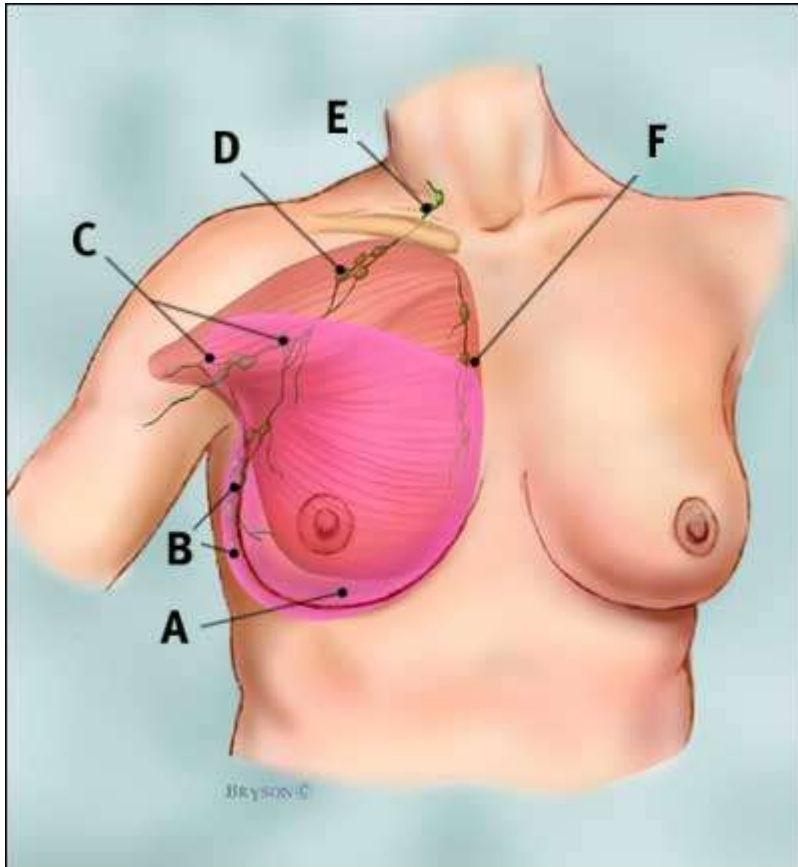
(Macrae/ Jung)

<i>author</i>	<i>year</i>	<i>prevalence</i>	<i>time</i>
<i>Jamison</i>	1979	<b>44%</b>	2 years
<i>Kroner</i>	1989	<b>23%</b>	1 year
<i>Vecht</i>	1990	<b>18%</b>	6 months
<i>Kroner</i>	1992	<b>17-31%</b>	6 years
<i>Ivens</i>	1992	<b>20%</b>	> 4 years
<i>Polinsky</i>	1994	<b>22-32%</b>	mean 8 years
<i>Tasmuth</i>	1995	<b>&gt;50%</b>	1 year
<i>Wallace</i>	1996	<b>22- 49%</b>	1 year
<i>Smith</i>	1999	<b>43%</b>	6 years
<i>Johansen</i>	2000	<b>15%</b>	6 years
<i>Fassoulaki</i>	2002	<b>33%</b>	3 months
<i>Reuben</i>	2004	<b>50%</b>	6 months
<i>Fassoulaki</i>	2005	<b>57%</b>	6 months
<i>Kairaluomma</i>	2006	<b>8%</b>	1 year

## **Nomenclature; post mastectomy pain syndrome**

- Chronic pain after **breast surgery**
- Chronic pain after **breast cancer treatment**
- Chronic pain in **breast cancer survivors**
  
- **Individual** pain conditions

# Types of breast surgery

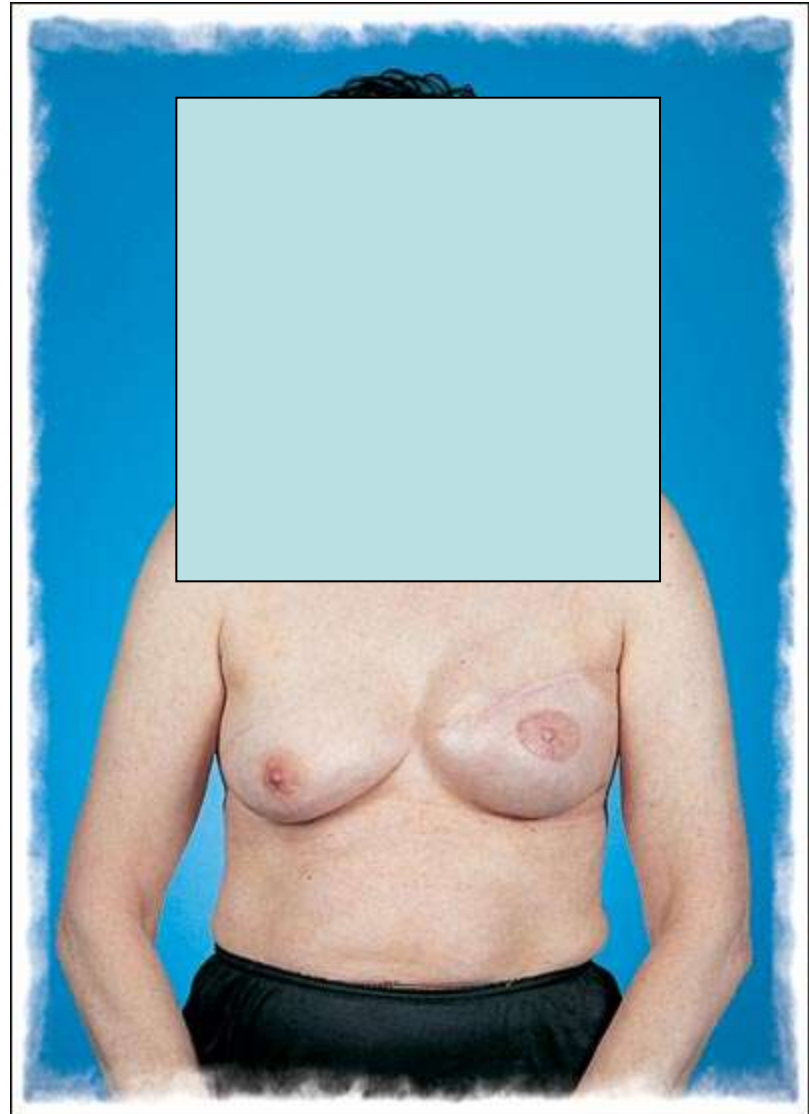
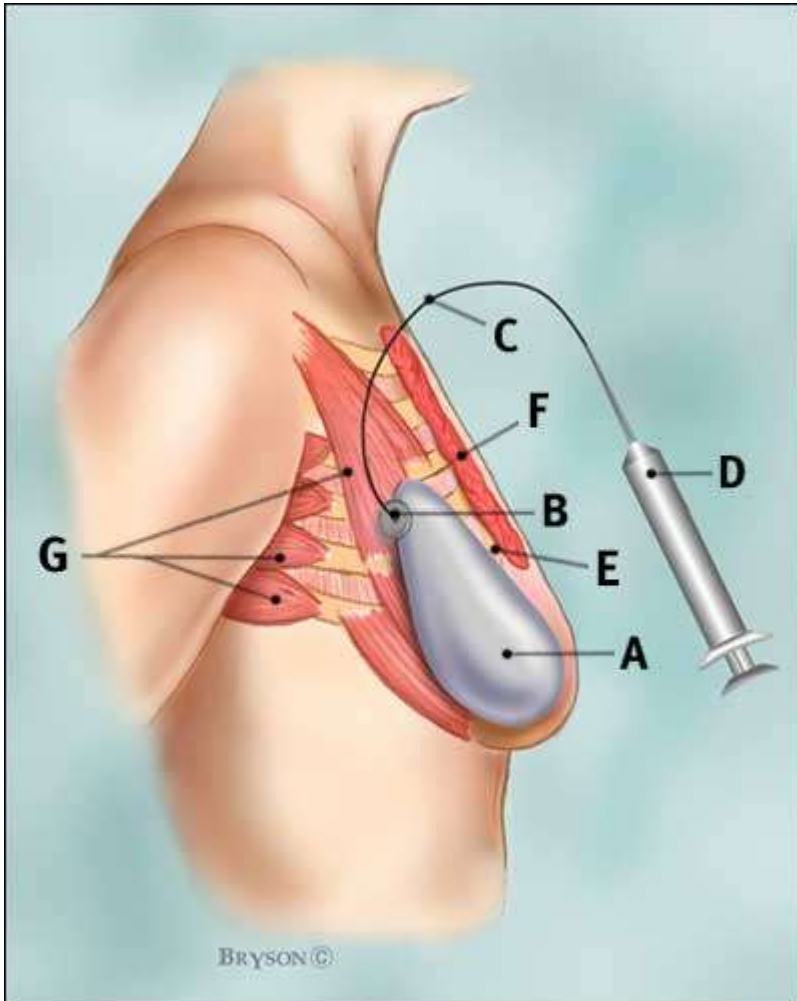


# Incidence of chronic pain after breast surgery

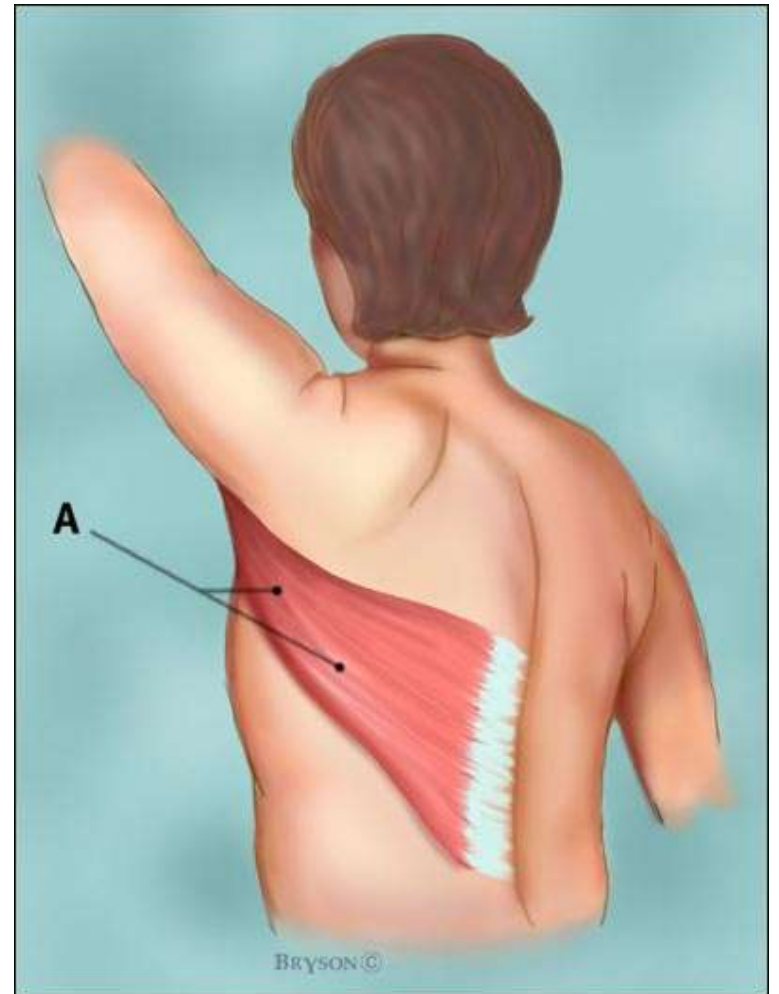
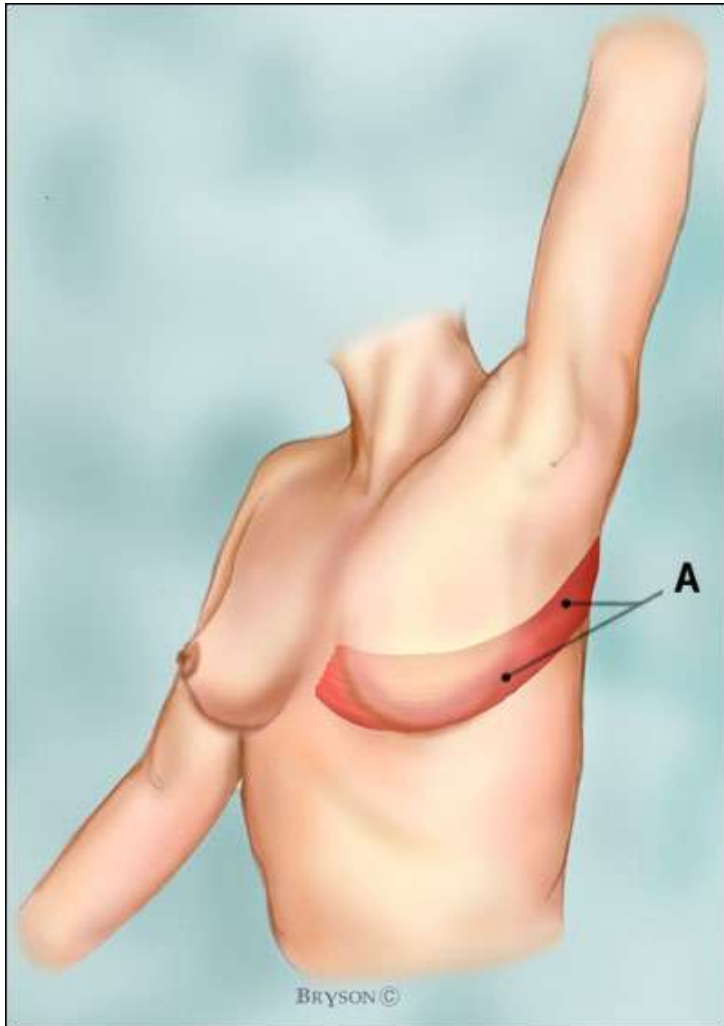
*Tasmuth et al, Ann Oncol 1995;6;453-9*

	<b>Time after surgery (months)</b>	<b>Prevalence %</b>
<b>mastectomy</b>	<b>32</b>	<b>28- 41</b>
<b>breast conserving</b>	<b>28</b>	<b>37- 61</b>

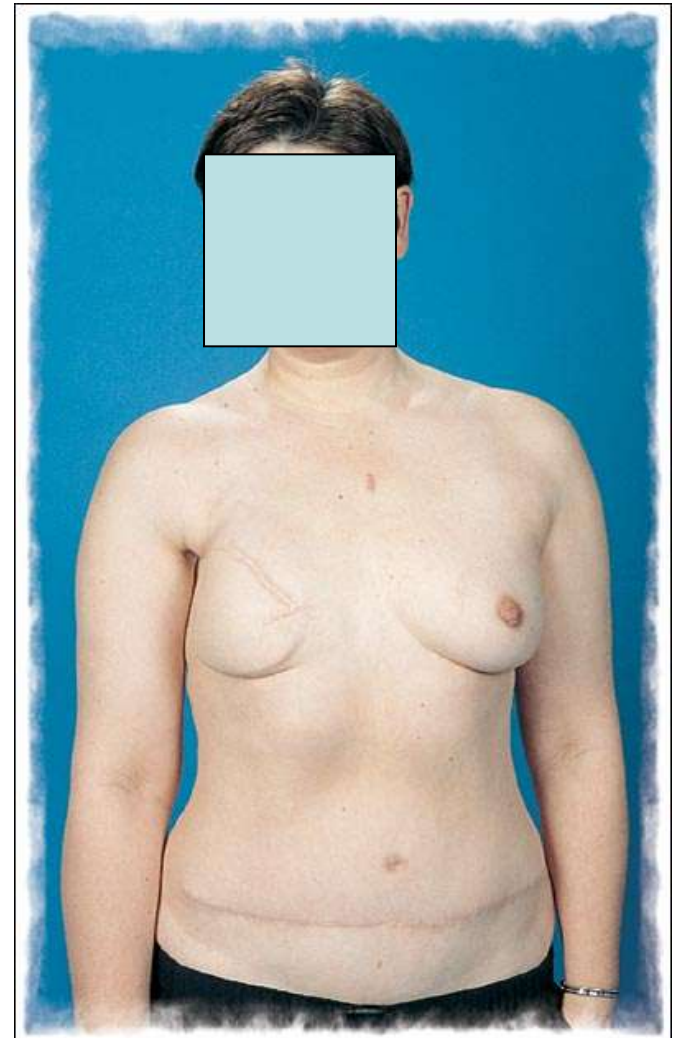
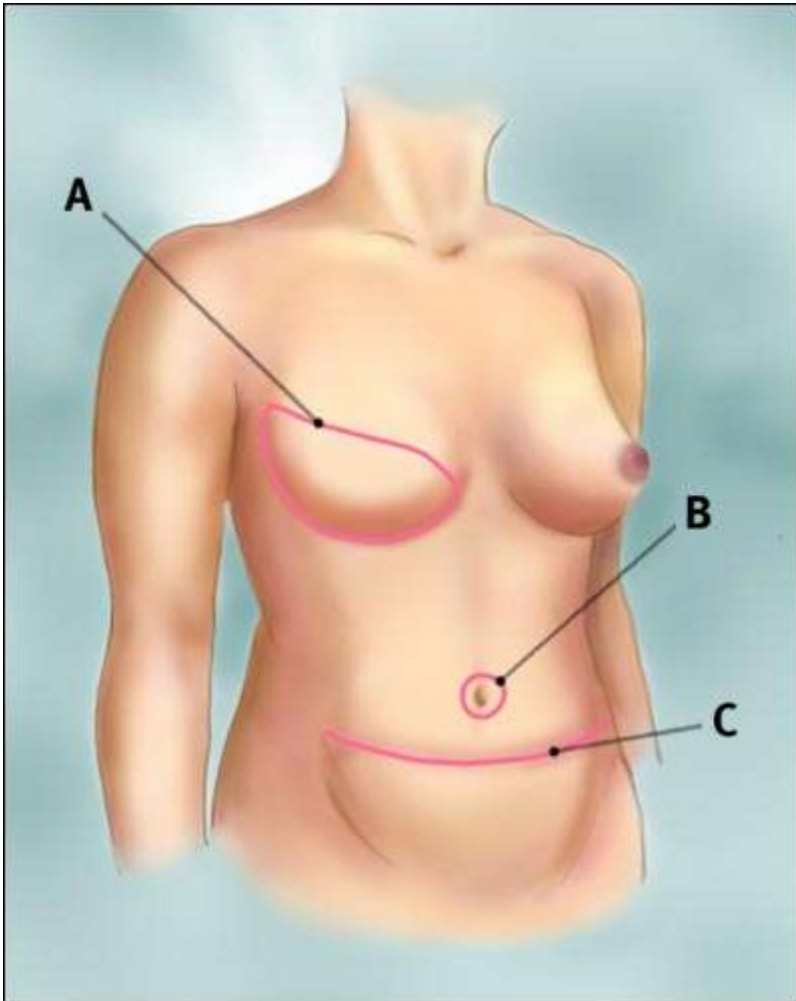
# Mastectomy & reconstruction



# Latissimus dorsi reconstruction



# TRAM-flap reconstruction



# Incidence of chronic pain after breast surgery

*Wallace et al, Pain 1996;6;195-205*

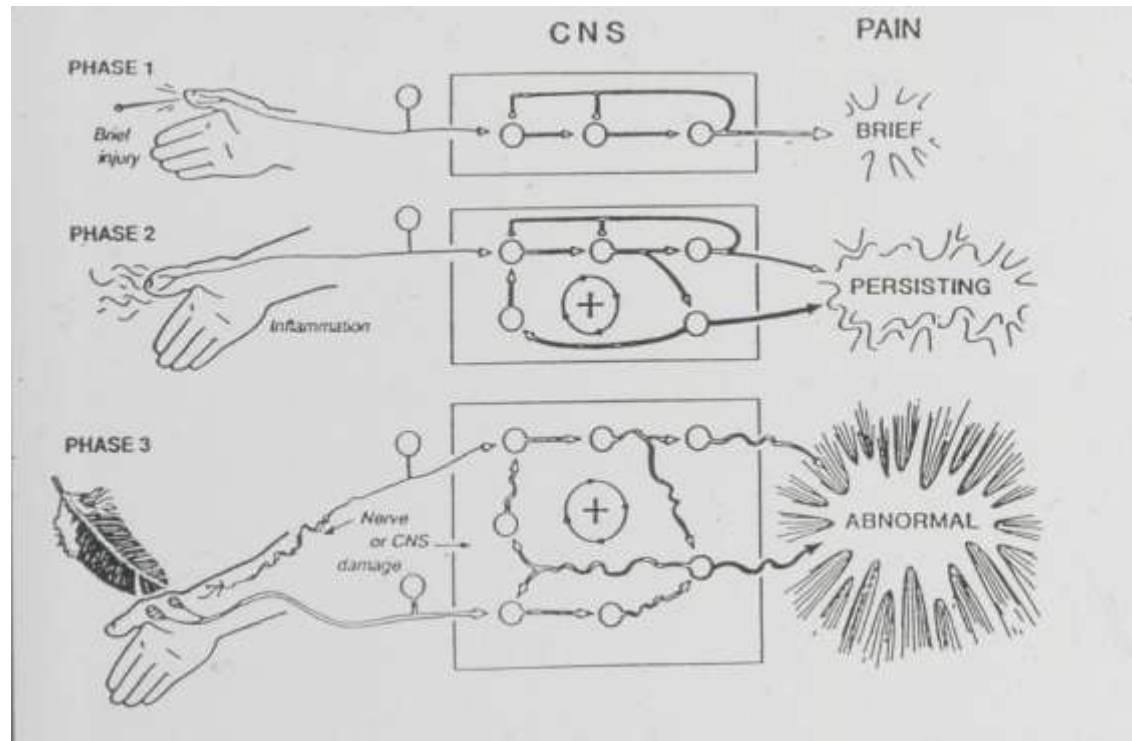
	<b>Prevalence % @ 1 year</b>
<b>mastectomy &amp; reconstruction</b>	<b>49</b>
<b>mastectomy</b>	<b>31</b>
<b>breast reduction</b>	<b>22</b>



# Neuropathic pain following breast cancer surgery: proposed classification and research update

*Jung et al, Pain 2003; 104:1-13*

1. Intercostobrachial
2. Phantom breast
3. Neuroma
4. Other nerve injury





# Neuropathic pain following breast cancer surgery: proposed classification and research update

*Jung et al, Pain 2003: 104:1-13*

## ***Other pains***

- Tumour recurrence
- Paraneoplastic processes
- Chemotherapy-associated neuropathy
- Radiation plexitis & plexopathy
- Persistent acute pain
- Implant-related
- Psychological & physical factors

## **Classification of *'post mastectomy'* pain**

### **1. Pre-existing pain**

Osteo/rheumatoid arthritis      Fibromyalgia  
Costo-chondritis                      Cervical radiculopathy

### **2. Tumour involvement**

Recurrence                              Metastasis  
Cervical radiculopathy due to tumour

### **3. Post-surgical**

Intercostobrachial neuralgia      Other neuralgias      Persistent  
'acute' pain      Scar pain      Phantom breast      Intercostal  
neuromas

### **4. Neuropathic**

Carpal tunnel syndrome      RIBP  
Transient brachial neuritis      Complex regional pain syndrome

### **5. Pain due to implants & reconstruction**

Capsulitis                      Capsular contraction and hardening  
Foreign body reaction      Referred pain      Implant migration  
Atypical chest pain syndrome      Reconstruction 'issues'

### **6. Other causes**

Psychological factors      Lymphoedema      Pericapsulitis  
Muscle spasm      'Shoulder pain'      Post-chemo      Post-  
radiotherapy      Idiopathic      Myofascial pain dysfunction  
syndrome



# Management of Adverse Effects following Breast Radiotherapy



Maher Committee  
The Royal College of Radiologists

# 1. Intercostobrachial neuralgia (originally known as Post Mastectomy Pain Syndrome)

Reference	Title	Comments
<i>Wood K. South Med J 1978; 71: 662–663.</i>	<b>Intercostobrachial nerve entrapment syndrome.</b>	First description
<i>Granek, Prov Am Soc Clin Oncol 1984; 3;122</i>	<b>Post-mastectomy pain syndrome, PMPS</b>	
<i>Foley, Med Clin Nor Am 1987;71:169-84</i>	<b>Pain syndromes in patients with cancer</b>	Classic article
<i>Vecht, JPSM 1990;5:109-17</i>	<b>Damage to intercostobrachial nerve</b>	Neurologists detailed description
<i>Paredes, Am J Surg 1990;160;525-8</i>	<b>More pain associated with intercostobrachial sectioning</b>	Surgical RCT
<i>Abdullah, Br J Surg 1998;85;1443-5</i>	<b>RCT, less pain, numbness, sensory changes in preservation group</b>	Surgical RCT

## Sensory nerve supply of breast

Intercostal nerves, T3-T6, medial + lateral cutaneous branches

Lateral cutaneous branch of intercostal T2, intercostobrachial nerve, upper medial arm

## 2. Phantom breast pain

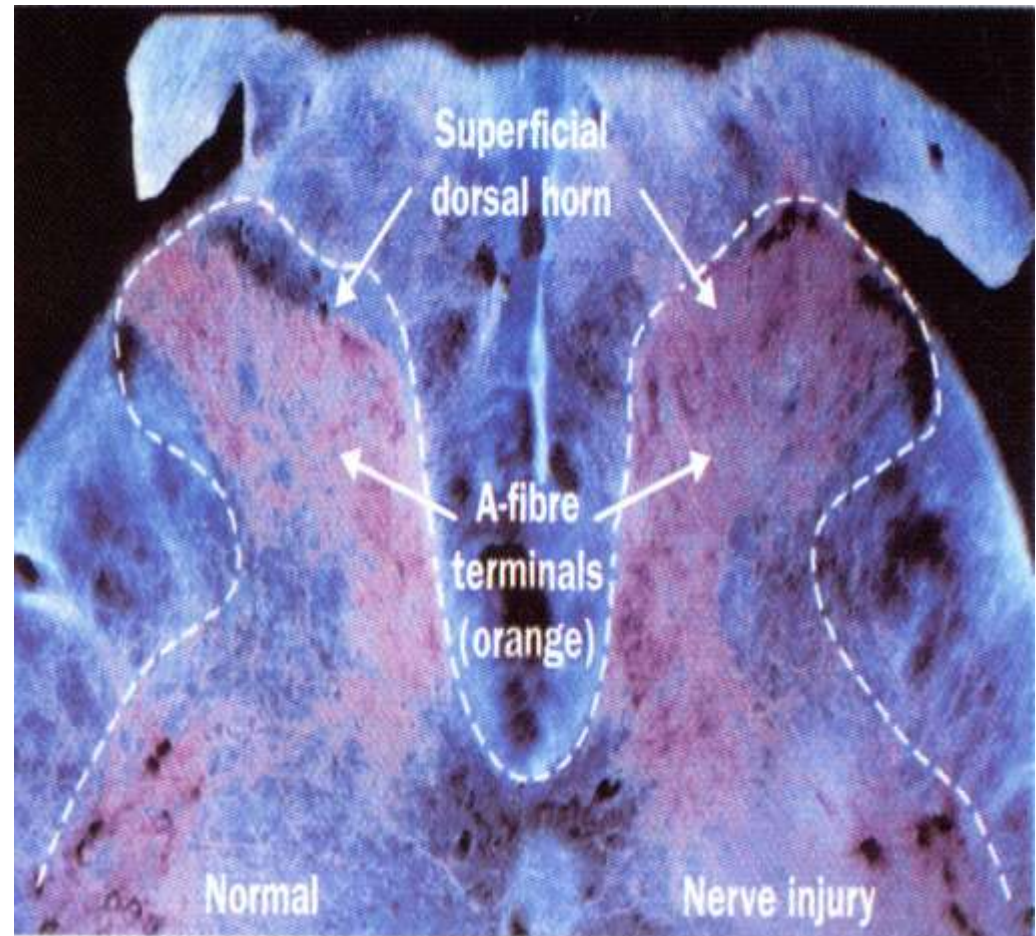
'sensory experience of a removed breast that is still present and is painful'

	<i>Time after surgery (months)</i>	<i>Prevalence %</i>
<i>Jamison 1979</i>	22	44
<i>Kroner 1989</i>	12	13
<i>Kroner 1992</i>	72	17

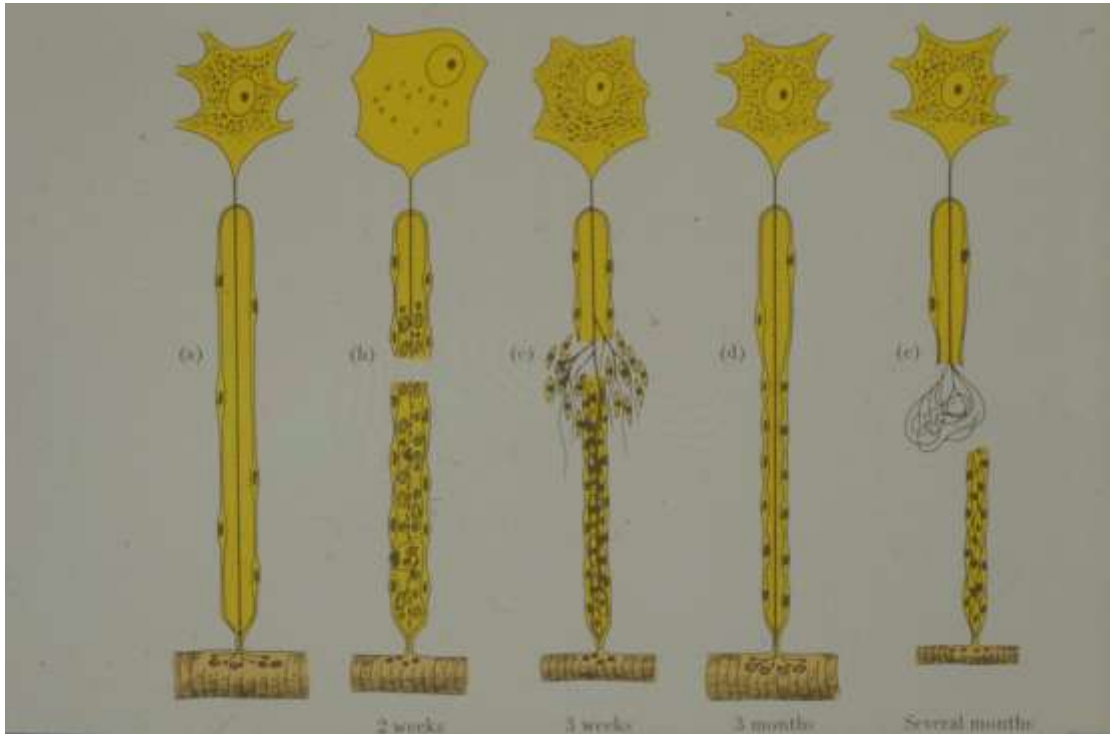


## Pathophysiological mechanisms: phantom breast pain

- Similar to any other phantom pain?
- Cortical imprint perpetuated by peripheral mechanisms?



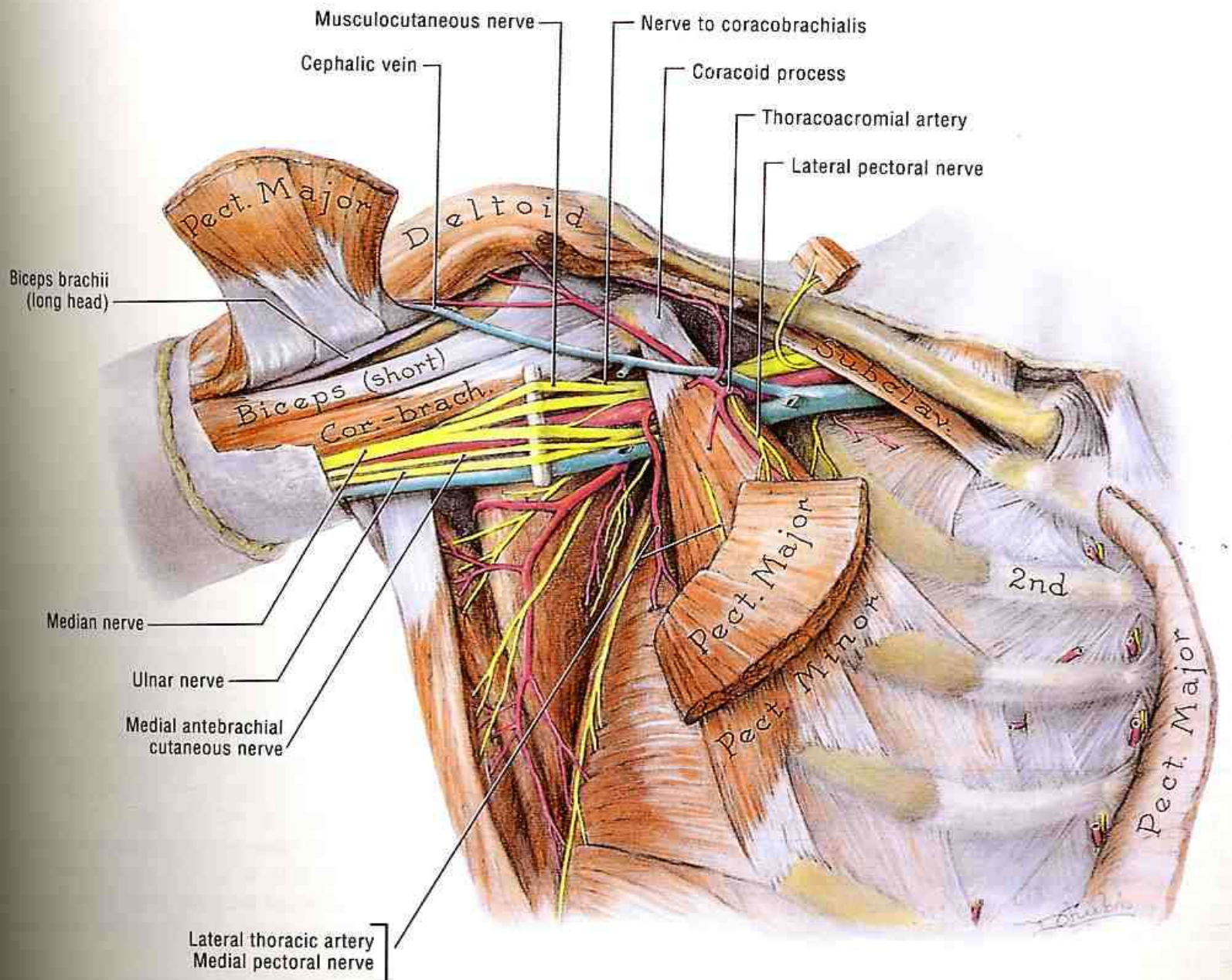
### 3. Neuroma pain - macro & micro neuromas



- Abnormal neuronal activity originating in trapped axons
- Source of ectopic discharge
- **Macroneuroma**- palpable mass of tangled axons
- **Microneuroma**- small numbers of axons- may not be palpable

## 4. Nerve damage from axillary dissection

- Intercostobrachial nerve
- Other intercostal nerves
- Medial cutaneous nerve of arm
  
- Sensory innervation around motor nerves  
(medial & lateral pectoral nerves, long thoracic, thoracodorsal)



**Figure 6-16.** Dissection of the pectoral region and axilla. The pectoralis major is reflected and the clavicular fascia is removed (also see Fig. 6-11).

## Prognosis/ Natural History

- Multiple sources of pain (RT, chemo, reconstruction, etc.)
- Natural or treatment effects?
- Some evidence for decrease over time



He was different from the other doctors.  
For one thing, he refused to play God.

## Prognosis

<i>Study</i>	<i>Initial assessment</i>	<i>Second assessment</i>
<i>Ivens 1992 chronic pain</i>	1-2 yrs – 31%	4 yrs – 20%
<i>Kroner 1989, 1992 phantom breast pain</i>	3 weeks - 50%,	6 years - 17%

Phantom breast sensations and phantom breast pain: A 2-year  
prospective study and a methodological analysis of literature

# **Long-term follow-up of breast cancer survivors with post-mastectomy pain syndrome**

*L Macdonald, J Bruce, N W Scott, W C S Smith and W A Chambers  
British Journal of Cancer 2005: 92; 225-230*

- **Previous study: 1996 prevalence rate = 43%, mean time since surgery 3 years**
- **This study: 2002 prevalence rate = 52%, mean time since surgery was 9 years**
- **48% women reported their PMPS had resolved since the previous survey in 1996**
- **Quality of life scores were significantly lower in women with persistent PMPS compared to those women whose pain had resolved.**
- **Risk factors = younger age and heavier weight**
- **Of women reporting PMPS in 1996, half of those surveyed in 2002 continued to experience PMPS at a mean of 9 years after surgery**



## Quality of Life

- *PMPS has negative impact on physical & psychosocial functioning in 50%* **Tasmuth 1995**
- *Significantly greater psychological & psychiatric morbidity compared to general population*  
**Maunsell 1993, Glover 1995, Miaskowski 1995, Tasmuth 1996, Carpenter 1998, Akechi 2001**
- Causal relationships can only be established by prospective studies to differentiate from psychosocial risk factors



## Specific risk factors for chronic pain after breast surgery

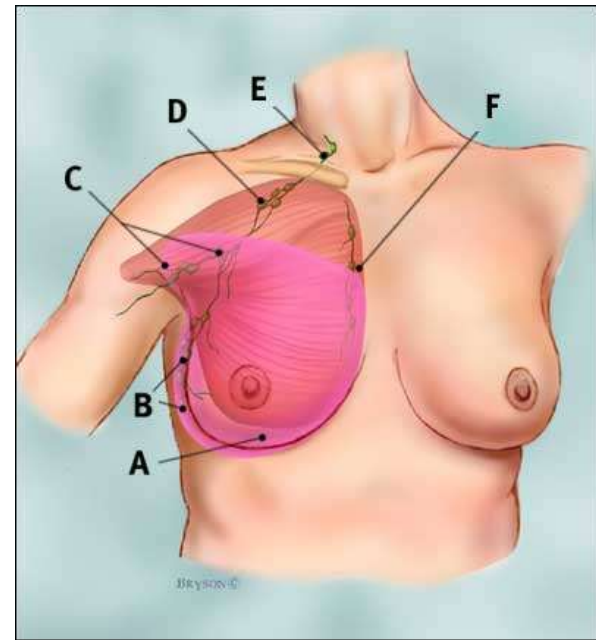
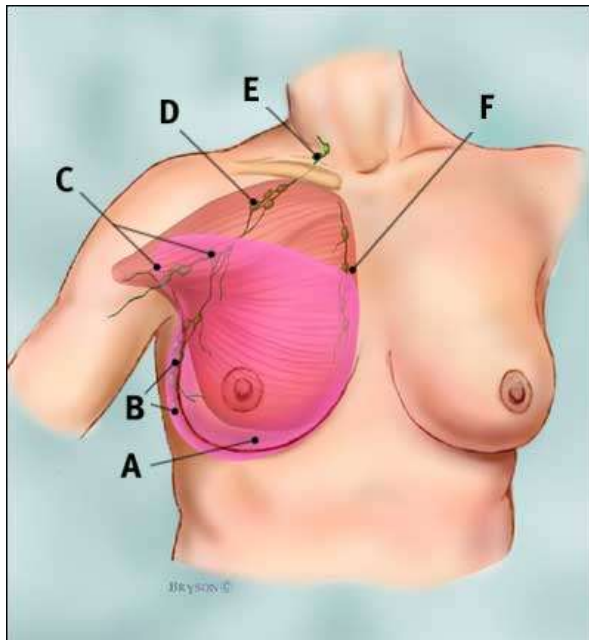
Younger patients	<i>de Vries 1994, Tasmuth 1995, Smith 1999</i>
No differences between age groups	<i>Kroner 1989, Ivens 1992, Carpenter 1999</i>
Chemotherapy	<i>Tasmuth 1995, Smith 1999</i>
Postoperative pain	<i>Tasmuth 1995, 1996, 1997, Jung 2002</i>
Preoperative anxiety/depression	<i>Tasmuth 1997</i>
Implants / reconstruction	<i>Wallace 1996</i>
Overweight	<i>Bosompra, 2002</i>
Surgical technique	<i>Abdullah 1998</i>

# Psychophysical examination in patients with post mastectomy pain.

*Gottrup et al. Pain 2000:87;275-84*

**Chronic Pain after breast surgery= 15**

**No Pain after breast surgery = 11**



# Pathophysiological mechanisms

- *Lower pain thresholds*
- *More cutaneous blood flow in pain patients*
- *More temporal summation, stimulus evoked pain & spontaneous pain*
  
- Similar to Post Herpetic Neuralgia  
*Central sensitisation by input from damaged primary afferents*  
*Rowbotham 1998*
  
- Mixed peripheral & central hypersensitisation  
*Woolf 1992*

# General treatment strategies for chronic postsurgical neuropathic pain

<p><b>Preventative</b></p> <p><i>Perkins &amp; Kehlet, Anesthesiology 2000</i></p>	<ul style="list-style-type: none"><li>•Surgical procedure, preservation, sentinel node biopsy</li><li>•Better postoperative pain management</li><li>•Informed consent / preparatory information</li></ul>
<p><b>Established</b></p> <p><i>Dworkin, Archives Neurol 2003: 60; 1524</i></p>	<ul style="list-style-type: none"><li>• Amitriptyline</li><li>•Gabapentin</li><li>•Opioids</li><li>•Tramadol</li><li>•5% Lidoderm patch</li></ul>

## Positive therapies for established PSBP

1. Pain management programme	<i>Robb 2006</i>
2. Capsaicin	<i>Watson 1989, 1992, Dini 1993</i>
3. Amitriptyline	<i>Kalso, 1995</i>
4. Venlafaxine	<i>Tasmuth, 2002</i>

# 1. A pain management programme for chronic cancer-treatment-related pain.

*Robb, Williams, Duvivier, Newham  
Journal of Pain 2006:7;75-150*

- Theory of cancer-related pain
- Pain pathways
- Over/under activity cycle
- Pacing
- Exercise and fitness
- TENS
- Posture and manual handling
- Relapse and prevention

## Psychology interventions

- Goal setting
- Role of factors involved in pain
- Homework assignments
- Relaxation techniques
- Cognitive skills
- Relapse and prevention



## Results

significant ( $p < 0.05$ ) improvements in:

- Pain severity
- Psychological distress
- Pain & psychological coping indices
- Activities of daily living
- General fitness

## 2. Topical Capsaicin for CPBS

8/14 good or excellent result	<i>Watson, Pain 1989:38;177-86</i>
RCT, Significant improvement in 2/4 outcome measures	<i>Watson, Pain 1992:5; 375-9</i>
2/21 complete relief, 11/21 – less pain	<i>Dini, Pain 1993:54;223-6</i>

### 3. Amitriptyline effectively relieves neuropathic pain following treatment of breast cancer

*Kalso, Pain 1995;64;293-302*

- 25mg – 100mg dose escalation over 4 weeks
- Significant reduction in neuropathic pain
- 8/15 had > 50% decrease in pain intensity
- Only 3 patients wanted to continue

## 4. Venlafaxine vs. placebo

*Tasmuth, Eur J Pain 2002:6;17-24*

- **Significant benefit from venlafaxine in 2/4 primary end-point measures**
- **No difference in adverse effects**

## Positive therapies for Prevention of PSBP

<b>1. EMLA</b> , applied to chest wall prior to surgery	<i>Fassoulaki, 2000</i>
<b>2. Venlafaxine</b> , before and for 2 weeks post surgery	<i>Reuben, 2004</i>
<b>3. Aggressive acute pain management</b>	<i>Iohom, 2006</i>
<b>4. Preincisional paravertebral block</b>	<i>Kairaluoma, 2006</i>

# 1. EMLA reduces acute and chronic pain after breast surgery for cancer

*Fassoulaki, Reg Anesth Pain Med 2000:25;350-5*

- **EMLA 20g** (on the chest & axilla before & 6 days after surgery) **vs. placebo**
- **2/5 post-op** measures better with EMLA
- **@ 3 months** less ( $p < 0.05$ ) chronic pain

## 2. Evaluation of the perioperative administration of Venlafaxine XR in the prevention of CPBS

*Reuben et al, J Pain & Symp Manage, 2004: 27;133-139*

- **Venlafaxine XR 70mg** for 2 weeks, starting night before surgery vs. **placebo**
- No differences in **acute pain** measures
- **Significantly less chronic pain @ 6 months;**

**3. The associations between severity of early postoperative pain, chronic postsurgical pain and plasma concentration of stable nitric oxide products after breast surgery.**

*Iohom et al, Anesthesia & Analgesia 2006*

Group 1. Standard analgesia

Group 2. Paravertebral block & 'aggressive' postop analgesia for 48 hours

- No patients in 'aggressive' group developed CPSP @ 10 weeks (12/15 in control group)
- Adequacy of postoperative analgesia is an important determinant of CPSP after breast surgery



## 4. Preincisional Paravertebral Block Reduces the Prevalence of Chronic Pain After Breast Surgery

*Kairaluoma, Bachmann, Rosenberg, Pere,  
Anesth Analg 2006;103:703-708*

- Preincisional **paravertebral block** provides significant immediate postoperative analgesia
- In the same patients ( $n = 60$ ), a 1-yr follow-up for chronic pain
- 12 months, less pain ( $P = 0.003$ ) in the PVB group.
- In addition to providing acute postoperative pain relief, preoperative PVB reduces the prevalence of chronic pain 1 yr after breast cancer surgery.

## Conclusions- chronic pain after breast surgery

1. Expanding 'survivor' population
2. Treat as a form of neuropathic pain
3. A model for ***acute to chronic*** transition  
informed consent, recognition of risk factors,  
preventative treatments