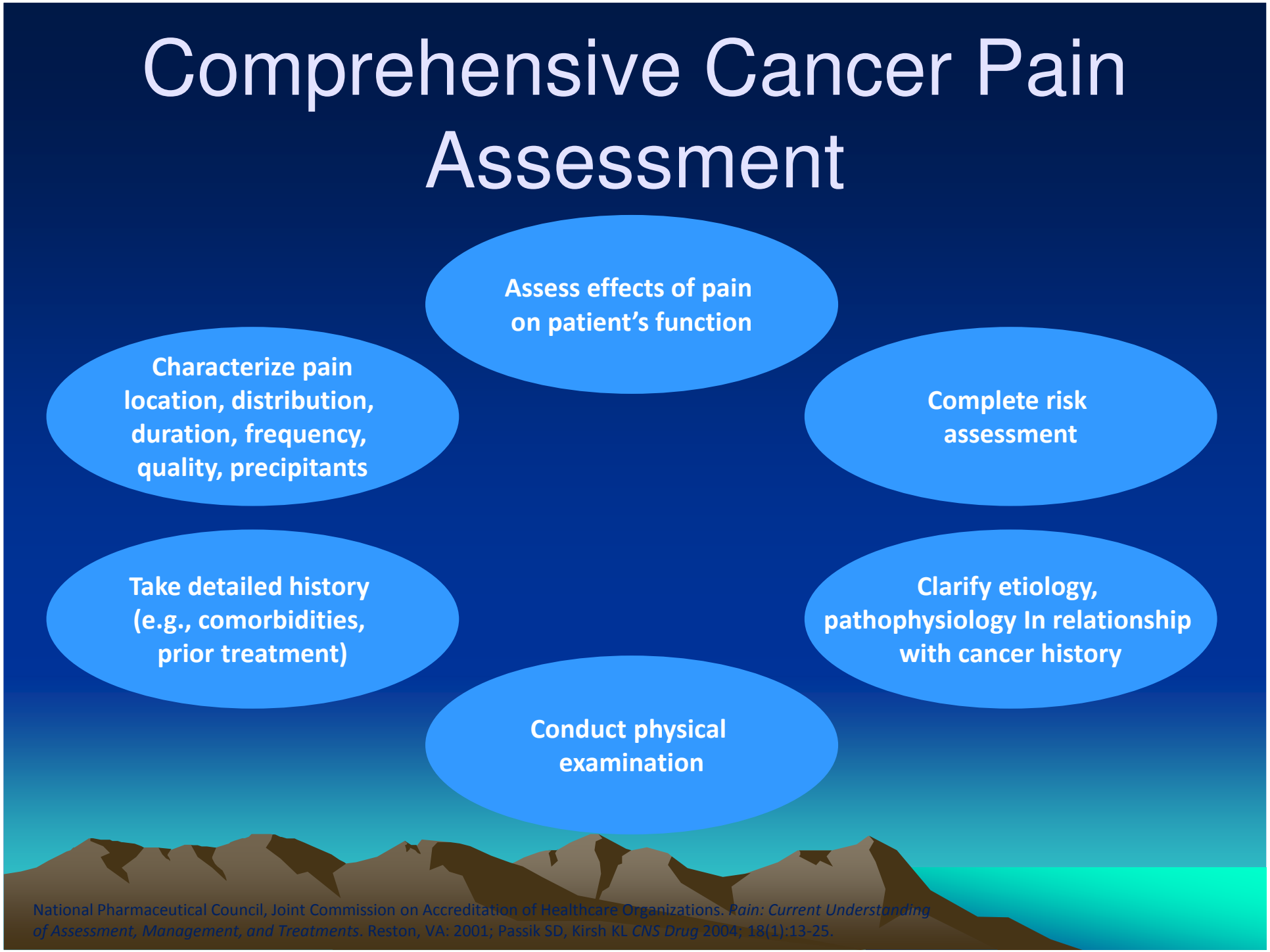
"Total pain " as defined by Mrs Hinson when admitted to St Jospeph Hospice

- " Well doctor, the pain began in my back, but now it seems that **all of me is wrong** My husband and son were marvellous but they were at work and they would have to stay off and loose their money. I could have cried for the pills and injections although I knew I shouln't. Everything seemed to be against me and nobody seemed to understand" … "But it's so wonderful to begin to feel **safe** again"

Cicely Sauders Nursing Mirror 1964; 14 February: pp vii-x

Comprehensive Cancer Pain Assessment



National Pharmaceutical Council, Joint Commission on Accreditation of Healthcare Organizations. *Pain: Current Understanding of Assessment, Management, and Treatments*. Reston, VA: 2001; Passik SD, Kirsh KL *CNS Drug* 2004; 18(1):13-25.

clinical practice guidelines

Annals of Oncology 23 (Supplement 7): vii139–vii154, 2012
doi:10.1093/annonc/mds233

Management of cancer pain: ESMO Clinical Practice Guidelines†

C. I. Ripamonti[1], D. Santini[2], E. Maranzano[3], M. Berti[4] & F. Roila[5], on behalf of the ESMO Guidelines Working Group*

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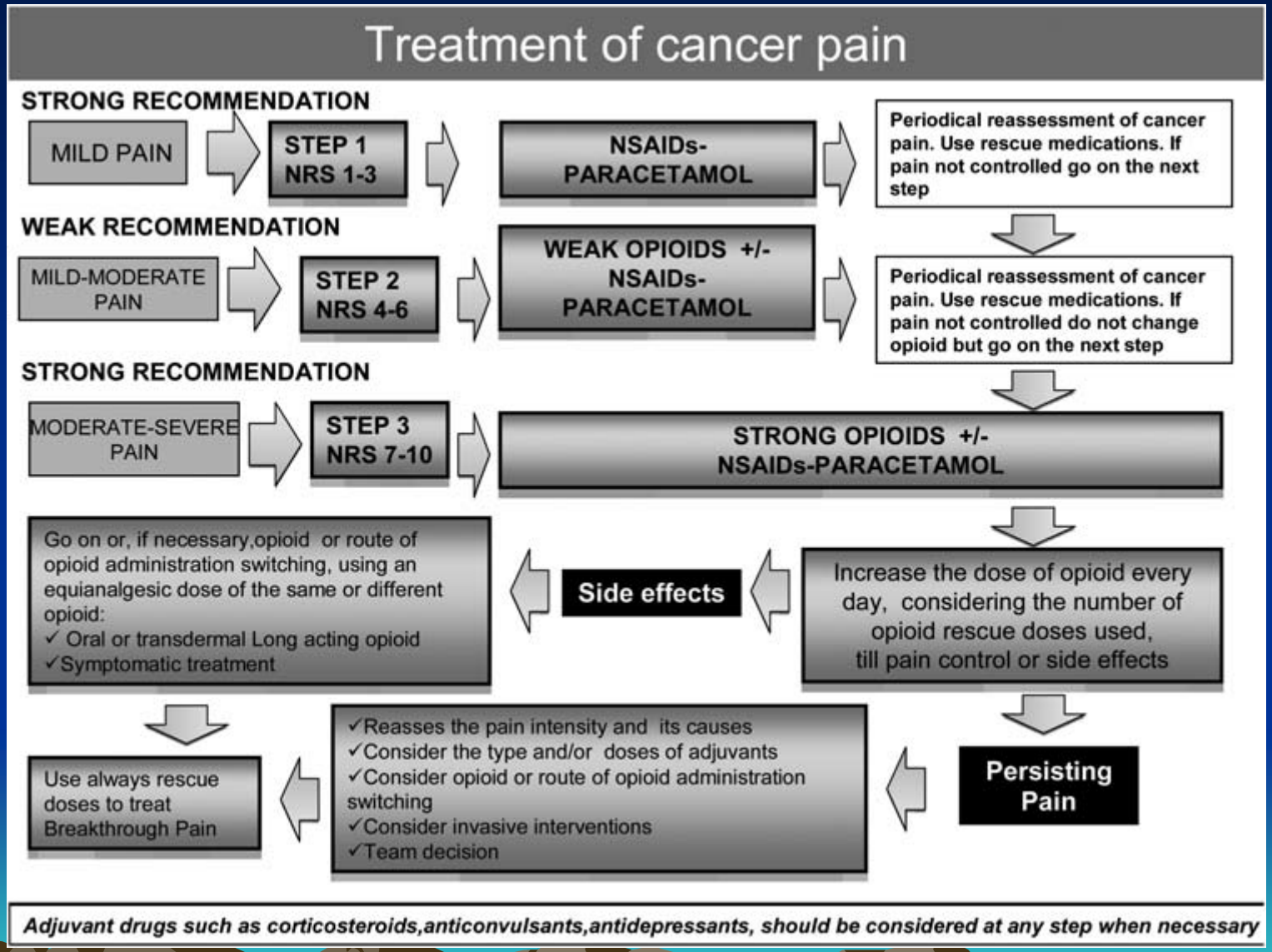

Treatment of cancer pain
STRONG RECOMMENDATION
MILD PAIN
STEP 1
NRS 1-3
NSAIDs-
PARACETAMOL
Periodical reassessment of cancer pain. Use rescue medications. If pain not controlled go on the next step
WEAK RECOMMENDATION
MILD-MODERATE PAIN
STEP 2
NRS 4-6
WEAK OPIOIDS +/-
NSAIDs-
PARACETAMOL
Periodical reassessment of cancer pain. Use rescue medications. If pain not controlled do not change opioid but go on the next step
STRONG RECOMMENDATION
MODERATE-SEVERE PAIN
STEP 3
NRS 7-10
STRONG OPIOIDS +/-
NSAIDs-PARACETAMOL
Increase the dose of opioid every day, considering the number of opioid rescue doses used, till pain control or side effects
Side effects
Go on or, if necessary,opioid or route of opioid administration switching, using an equianalgesic dose of the same or different opioid:
✓ Oral or transdermal Long acting opioid
✓Symptomatic treatment
Persisting Pain
✓Reasses the pain intensity and its causes
✓Consider the type and/or doses of adjuvants
✓Consider opioid or route of opioid administration switching
✓Consider invasive interventions
✓Team decision
Use always rescue doses to treat Breakthrough Pain
Adjuvant drugs such as corticosteroids,anticonvulsants,antidepressants, should be considered at any step when necessary

Review

Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC

Augusto Caraceni, Geoffrey Hanks*, Stein Kaasa*, Michael I Bennett, Cinzia Brunelli, Nathan Cherny, Ola Dale, Franco De Conno, Marie Fallon, Magdi Hanna, Dagny Faksvåg Haugen, Gitte Juhl, Samuel King, Pål Klepstad, Eivor A Laugsand, Marco Maltoni, Sebastiano Mercadante, Maria Nabal, Alessandra Pigni, Lukas Radbruch, Colette Reid, Per Sjogren, Patrick C Stone, Davide Tassinari, Giovambattista Zeppetella, for the European Palliative Care Research Collaborative (EPCRC), on behalf of the European Association for Palliative Care (EAPC)*

Here we provide the updated version of the guidelines of the European Association for Palliative Care (EAPC) on the use of opioids for the treatment of cancer pain. The update was undertaken by the European Palliative Care Research Collaborative. Previous EAPC guidelines were reviewed and compared with other currently available guidelines, and consensus recommendations were created by formal international expert panel. The content of the guidelines was defined according to several topics, each of which was assigned to collaborators who developed systematic literature reviews with a common methodology. The recommendations were developed by a writing committee that combined the evidence derived from the systematic reviews with the panellists' evaluations in a co-authored process, and were endorsed by the EAPC Board of Directors. The guidelines are presented as a list of 16 evidence-based recommendations developed according to the Grading of Recommendations Assessment, Development and Evaluation system.

Lancet Oncol 2012; 13: e58–68

*These authors contributed equally

Palliative Care, Pain Therapy and Rehabilitation, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy (Prof A Caraceni MD, C Brunelli ScD, A Pigni MD); **Department of Palliative Medicine, Bristol Haematology**

Nociception, Pain and Suffering

Nociception : the activity produced in the nervous system by potentially tissue damaging stimuli

Pain "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”

Cancer pain pathophysiology

NOCICEPTIVE PAIN

Physiological appropriate Response to pain stimuli

NEUROPATHIC PAIN

Inappropriate response due to lesion or dysfunction of sensory system

Merskey, 1986.

Differential diagnosis

Site	Due to cancrer	Esiti
Upper limb	Brachial plexopathy Bone mets	PostRT plexopathy postaxillary dissection
Lower limb	L/S plexopathy radiculopathy bone mets	Plessopatie postattiniche e lesioni chirurgiche
Chest pain	Thoraci wall infiltration	Postthoracotomy pain
Trigeminal	Infiltrazione periferica e base cranica	Ch. Demolitiva e esiti RT
Head/neck shoulder	Local infiltration	Post surgery post RT
Visceral perineal pain	Presacral recurrency	Postsurgical

Pain due to different tissue etiologies

- Viscerale Nociceptive
- Somatic nociceptive
- Nervous tissue involvement by compression or infiltration
  - Neuropathic and non neuropathic

Paper II

PAIN® 155 (2014) 2707–2713

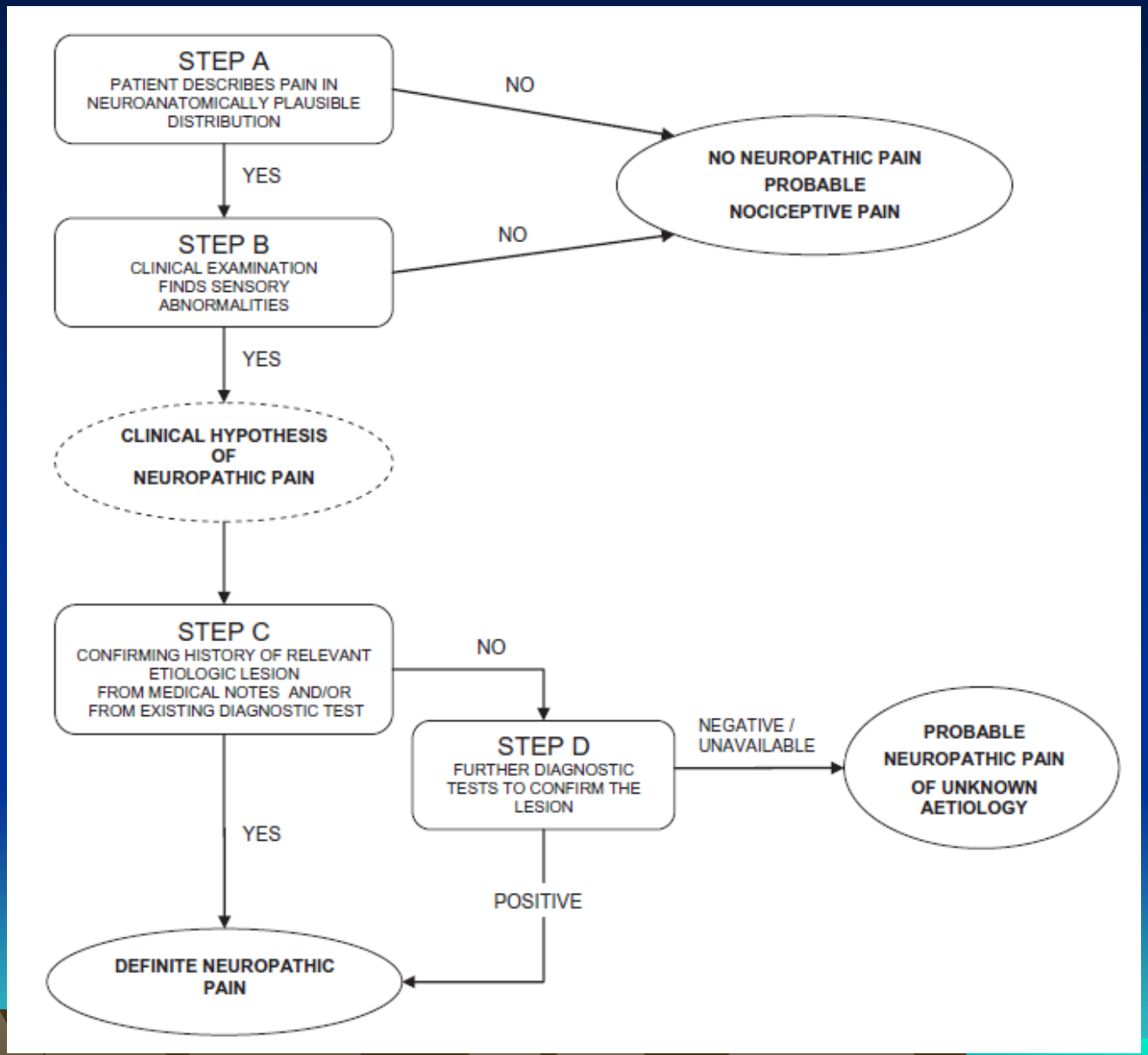
PAIN®

www.elsevier.com/locate/pain

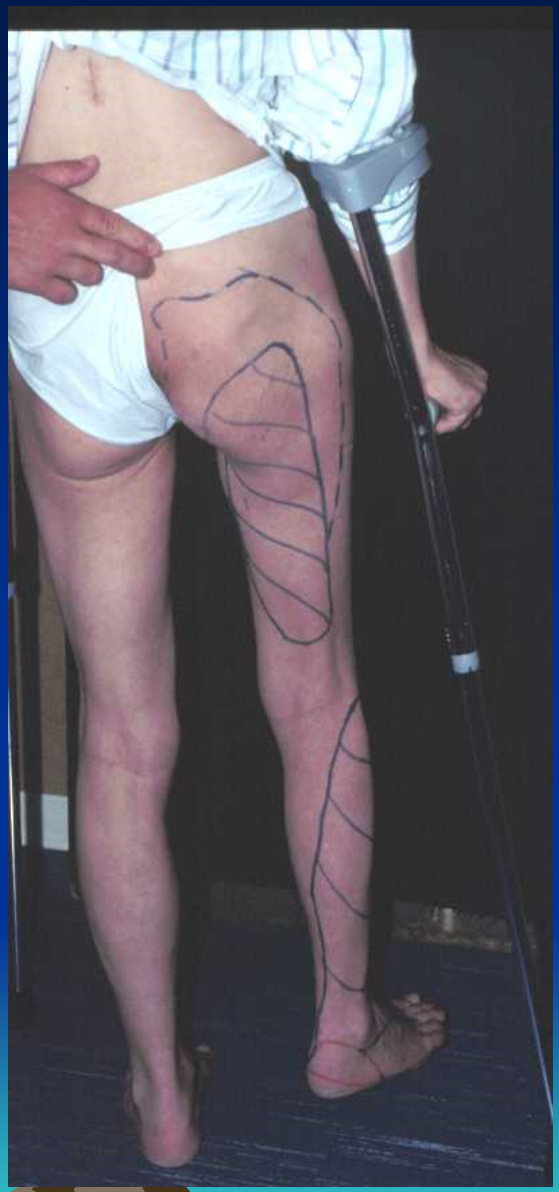
Classification of neuropathic pain in cancer patients: A Delphi expert survey report and EAPC/IASP proposal of an algorithm for diagnostic criteria

Cinzia Brunelli [a,b,*], Michael I. Bennett [c], Stein Kaasa [b,d], Robin Fainsinger [e], Per Sjøgren [f], Sebastiano Mercadante [g], Erik T. Løhre [b,d], Augusto Caraceni [a,b], on behalf of the European Association for Palliative Care (EAPC) Research Network, the International Association for the Study of Pain (IASP) Cancer Pain Special Interest Group

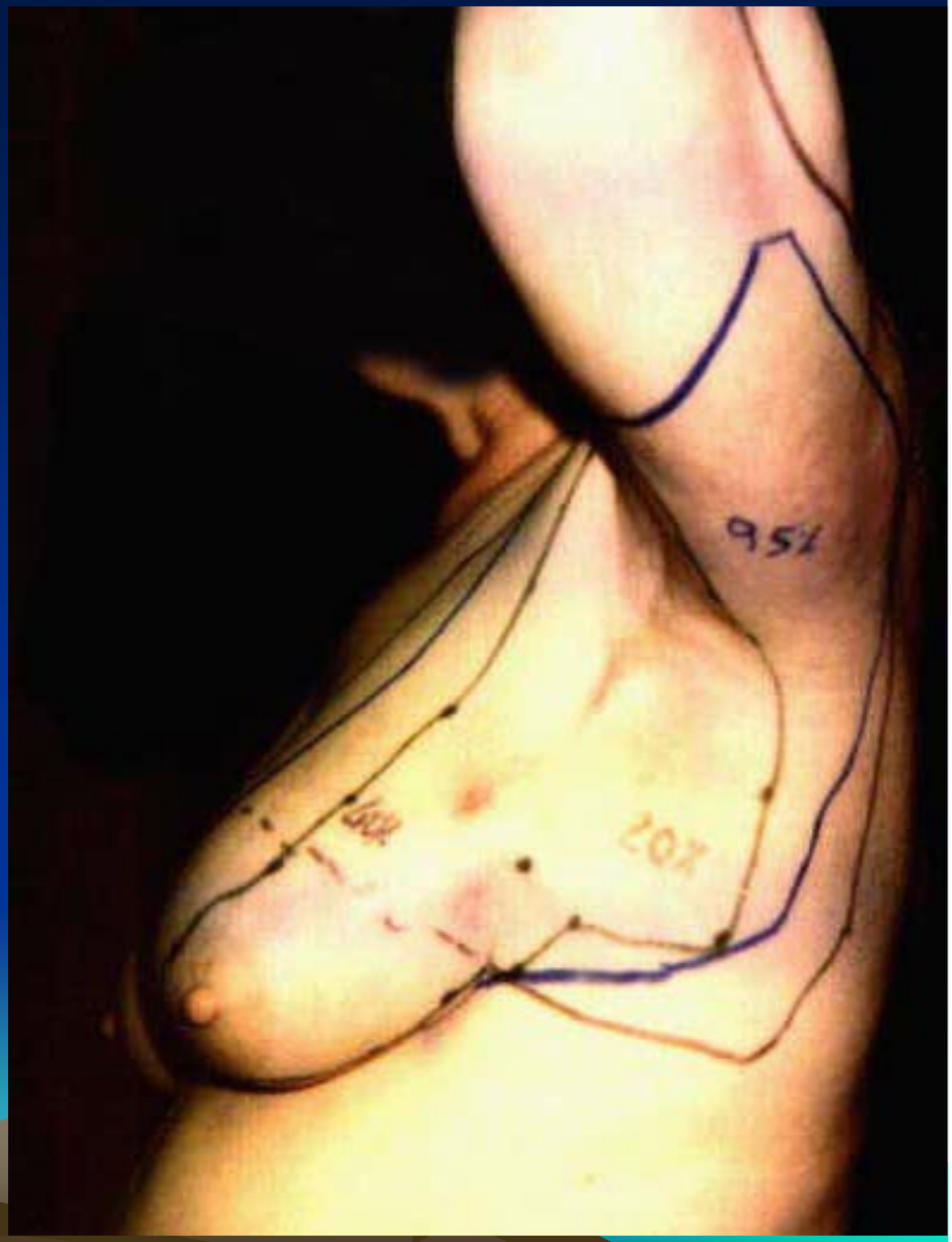
[a] *Palliative Care, Pain Therapy and Rehabilitation Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy*
[b] *European Palliative Care Research Centre (PRC), Department of Cancer Research and Molecular Medicine, Faculty of Medicine, Norwegian University of Science and Technology (NTNU), Trondheim, Norway*
[c] *Academic Unit of Palliative Care, Leeds Institute of Health Sciences, University of Leeds, Leeds, West Yorkshire, UK*
[d] *Cancer Clinic, St. Olavs Hospital, University Hospital of Trondheim, Trondheim, Norway*
[e] *Division of Palliative Care Medicine Department of Oncology, University of Alberta, Edmonton, AB, Canada*
[f] *Section of Palliative Medicine, Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark*
[g] *Anesthesia and Intensive Care & Pain Relief and Palliative Care Unit, la Maddalena Cancer Center, Palermo and University of Palermo, Palermo, Italy*


STEP A
PATIENT DESCRIBES PAIN IN NEUROANATOMICALLY PLAUSIBLE DISTRIBUTION
NO
YES
NO NEUROPATHIC PAIN
PROBABLE
NOCICEPTIVE PAIN
STEP B
CLINICAL EXAMINATION FINDS SENSORY ABNORMALITIES
NO
YES
CLINICAL HYPOTHESIS
OF
NEUROPATHIC PAIN
STEP C
CONFIRMING HISTORY OF RELEVANT ETIOLOGIC LESION FROM MEDICAL NOTES AND/OR FROM EXISTING DIAGNOSTIC TEST
NO
STEP D
FURTHER DIAGNOSTIC TESTS TO CONFIRM THE LESION
NEGATIVE / UNAVAILABLE
PROBABLE
NEUROPATHIC PAIN
OF UNKNOWN
AETIOLOGY
YES
POSITIVE
DEFINITE NEUROPATHIC
PAIN

- Neuropathic pain
  - Neurological lesion
  - Lancinating pain
  - Burning pain
  - Dysesthesia
  - Allodynia Hyperalgesia



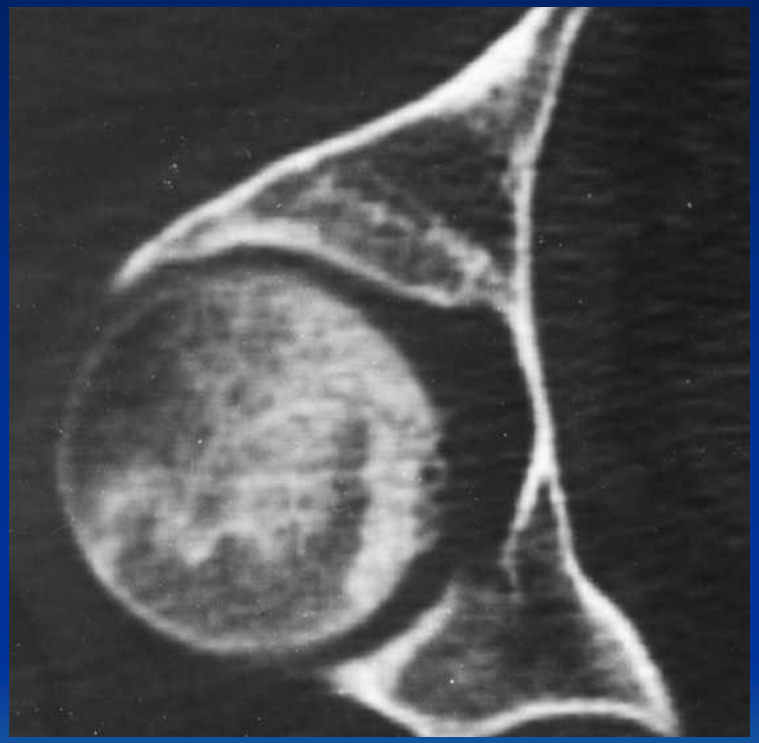
Sindrome del nervo Intercostobrachiale



Cortesia P Marchettini, M Lacerenza, F Formaglio Centro Medicina del Dolore S. Raffaele Ville Turro

Chronic pain due to cancer therapy

- Chemioterapie e farmaci
  - Polineuropatie
    - Cisplatino
    - Taxolo
    - Vincristina
    - Oxaliplatino
  - Psudoreumatismo da steroidi
  - Necrosi asettica ossea
  - Sindrome spalla mano da gardenale

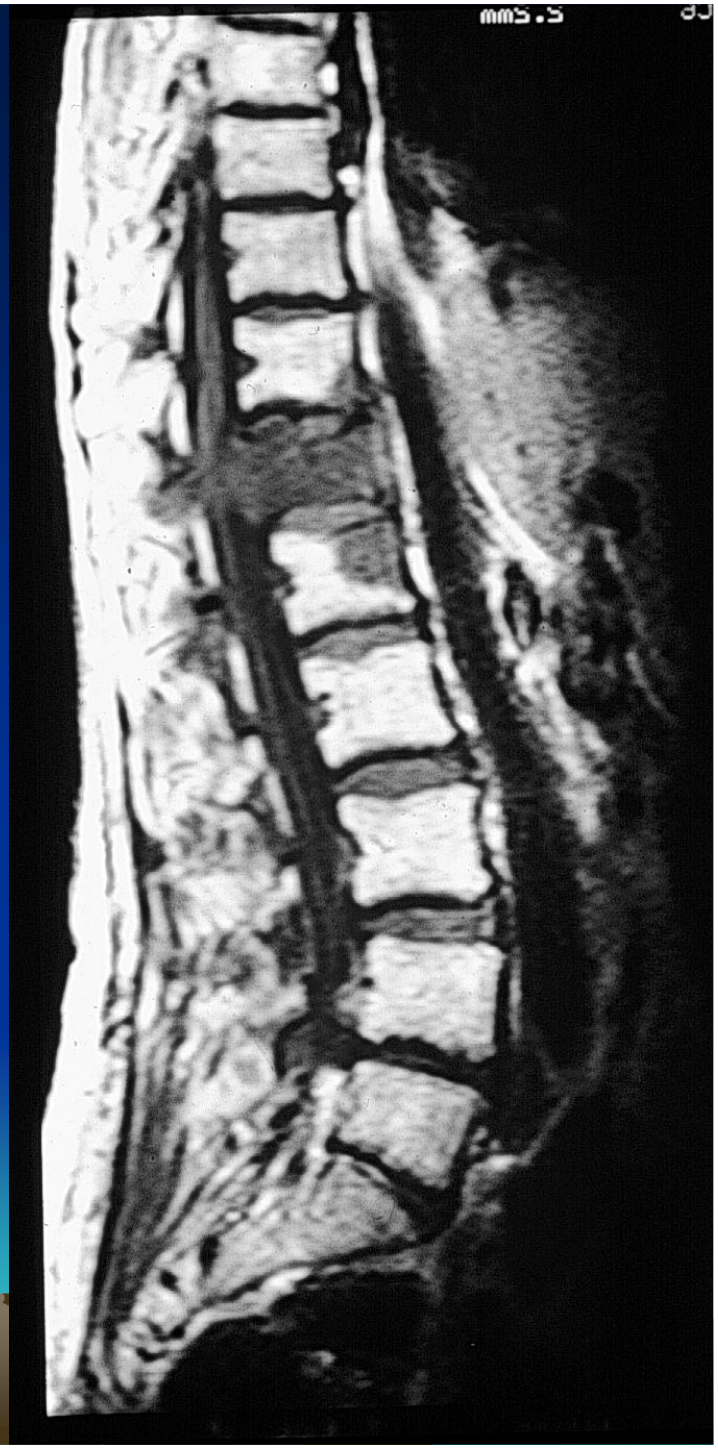


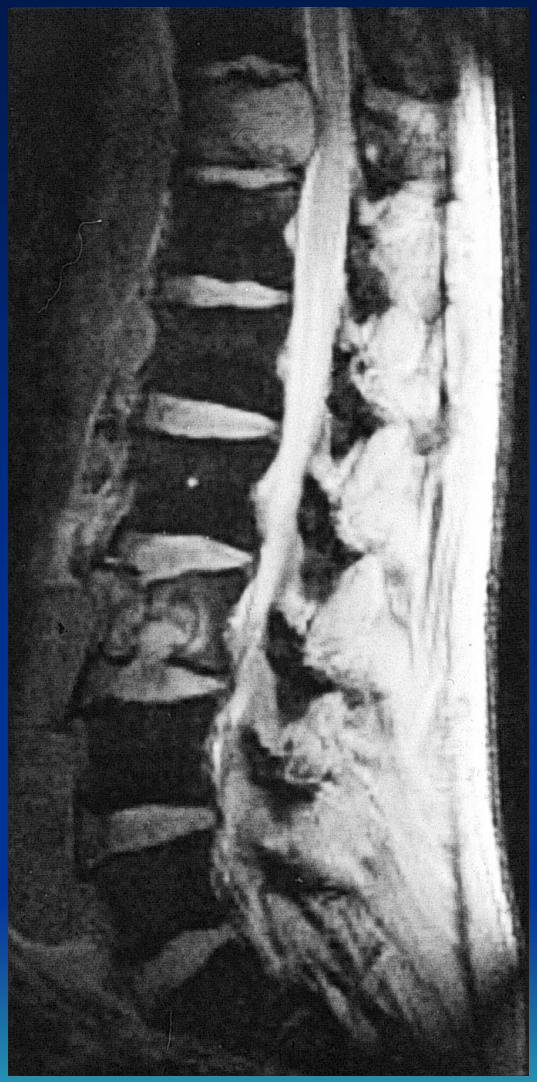
Cancer pain syndromes

- Bone lesion 41.7%
- Neurological lesion 30%
- Visceral lesion 28%
- Soft tissue lesion 20%

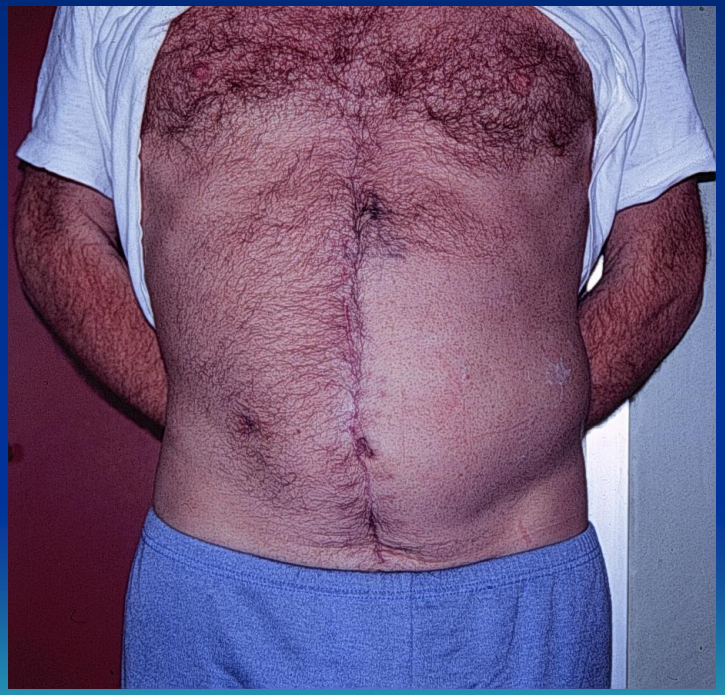
Caraceni et al Pain 1999

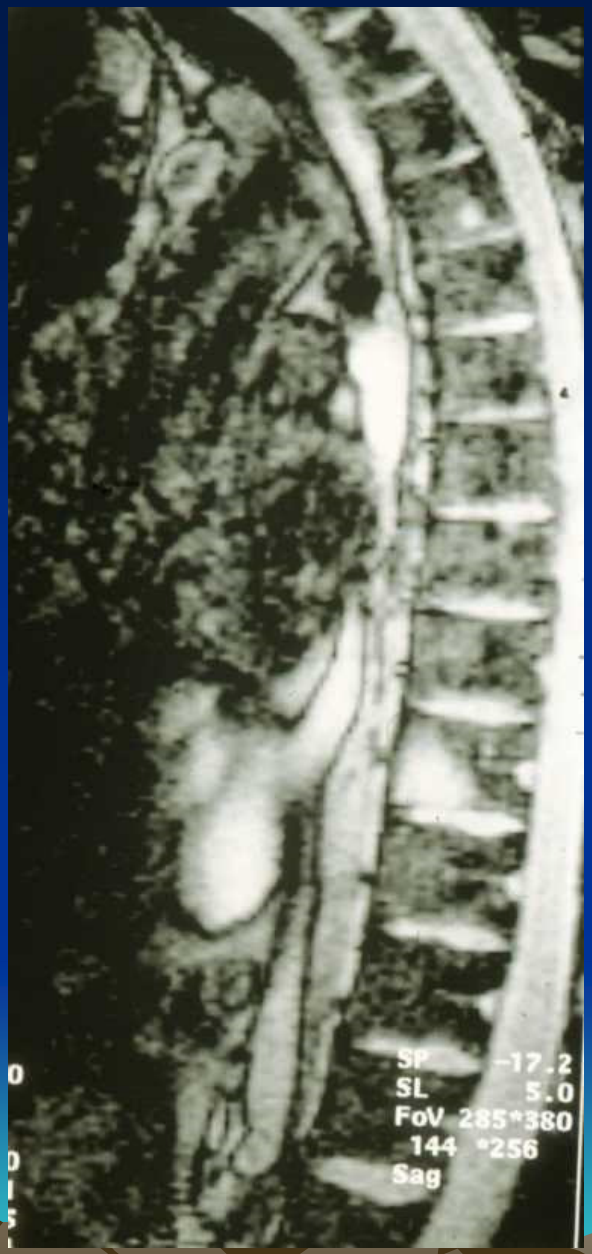
Referred bone pain
from D12 metastasis
with epidural extension



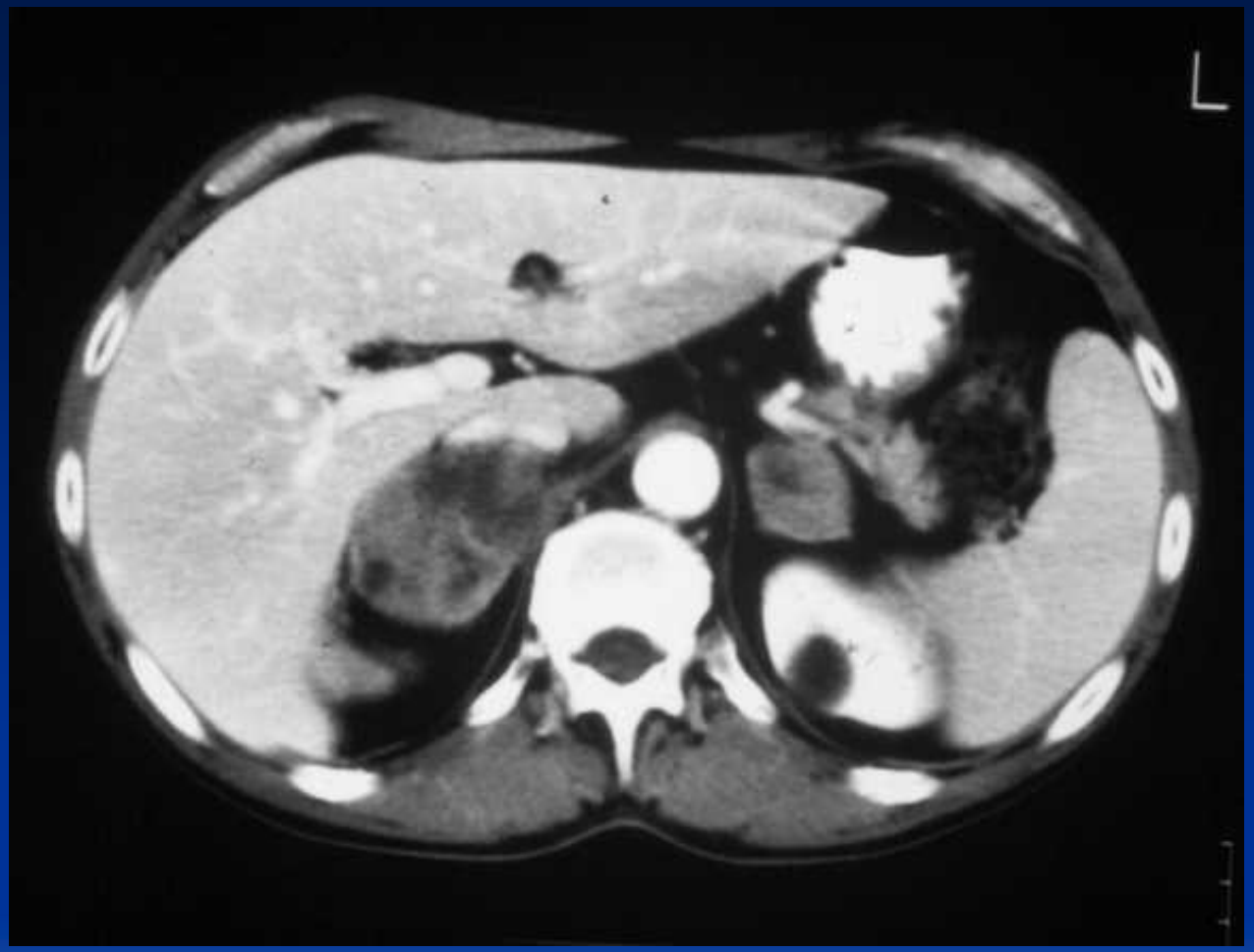


Colon carcinoma back pain and D11 radiculopathy





RMN
Melanoma



Lung cancer adrenal metastasis

Report of a case

Do EAPC guidelines fit in ?

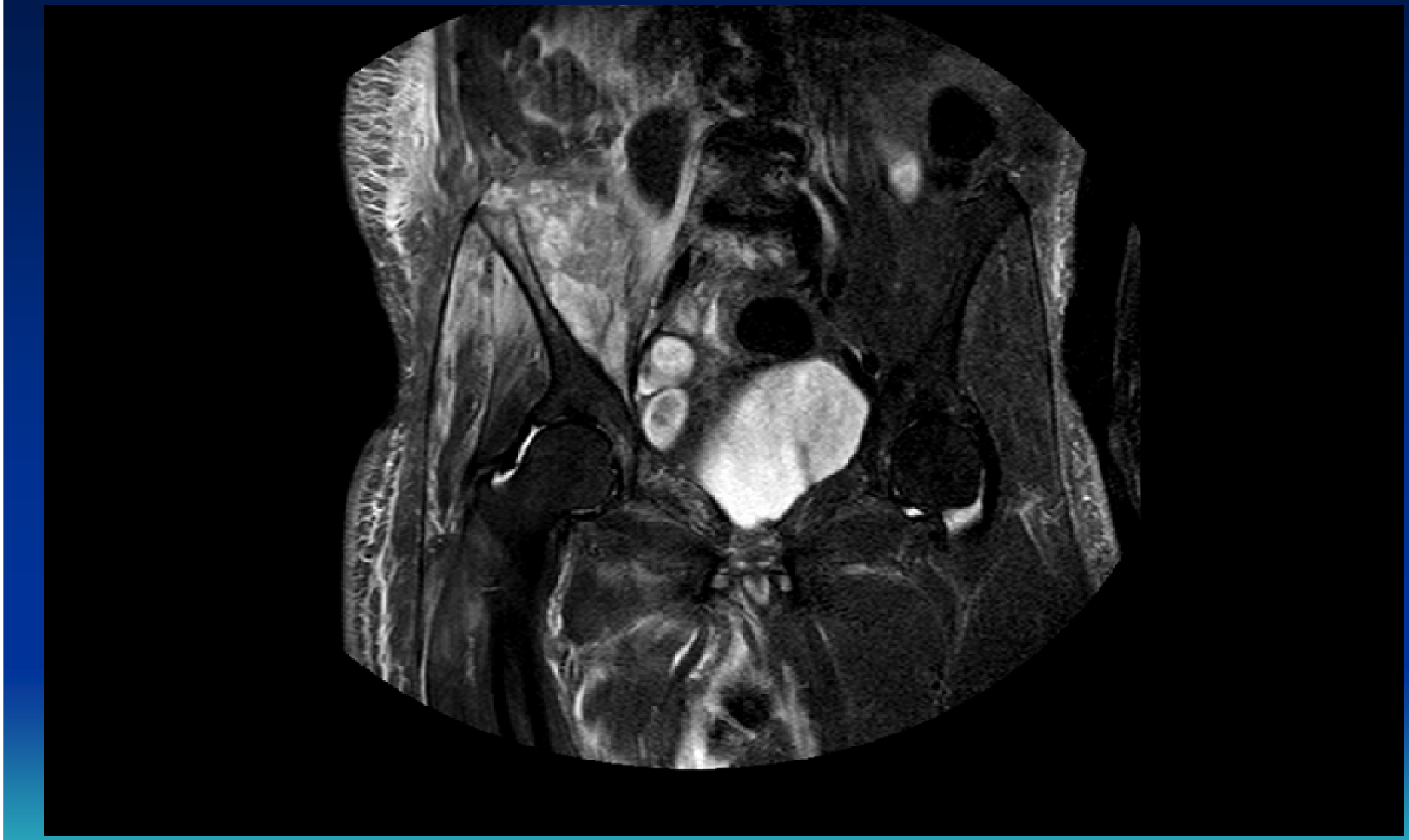
Do they help ?

Case history

- 01/02/2010 Urtelial Ca Bladder pT2G3
- 31/05/2010 Radical cystectomy (n-)
- June-Sept 2011 MVAC followed by TPG
- Vinflunine
- March 2012 Pazopanib
- May-June 2012 RT to right iliac bone
- Everolimus
- September 2012 worsening pain oxycodone and TTS fentanyl

24/01/2013 Palliative care clinic

- Continuous pain right emipelvis radiatingto all right lower limb
- Increases when sitting better on standing and laying down
- Shooting pain episodes, numbness in the leg and burnin pain in the upper right thigh
- Neurological sensory-motor signs
- Righ leg lymphedema
- 4/10



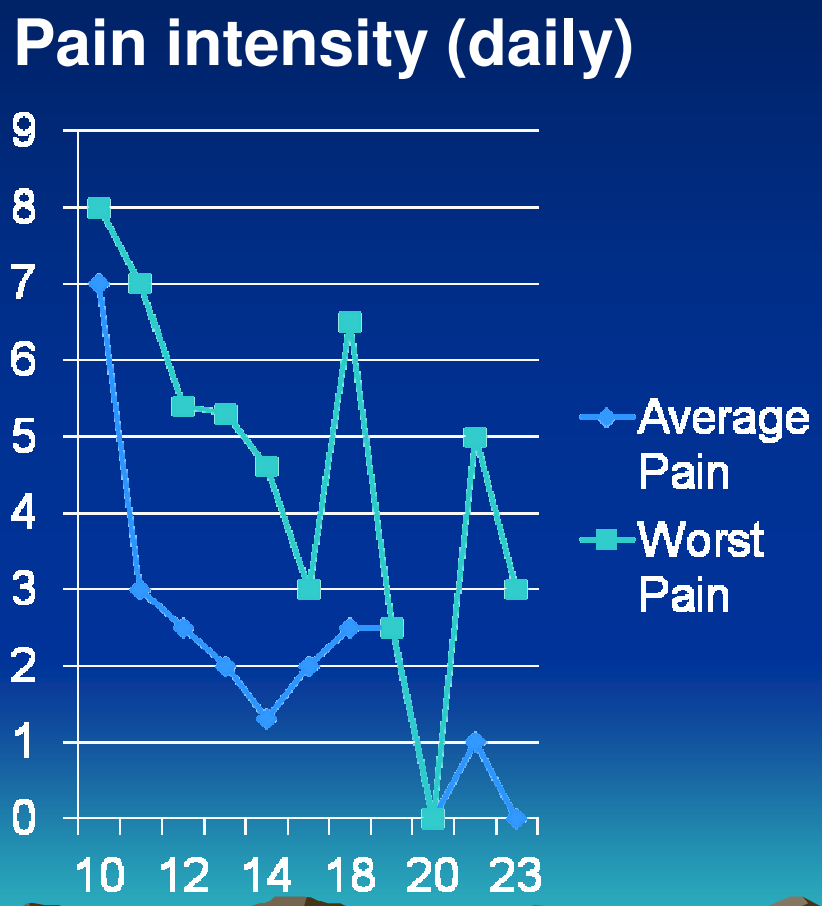
Palliative care clinic

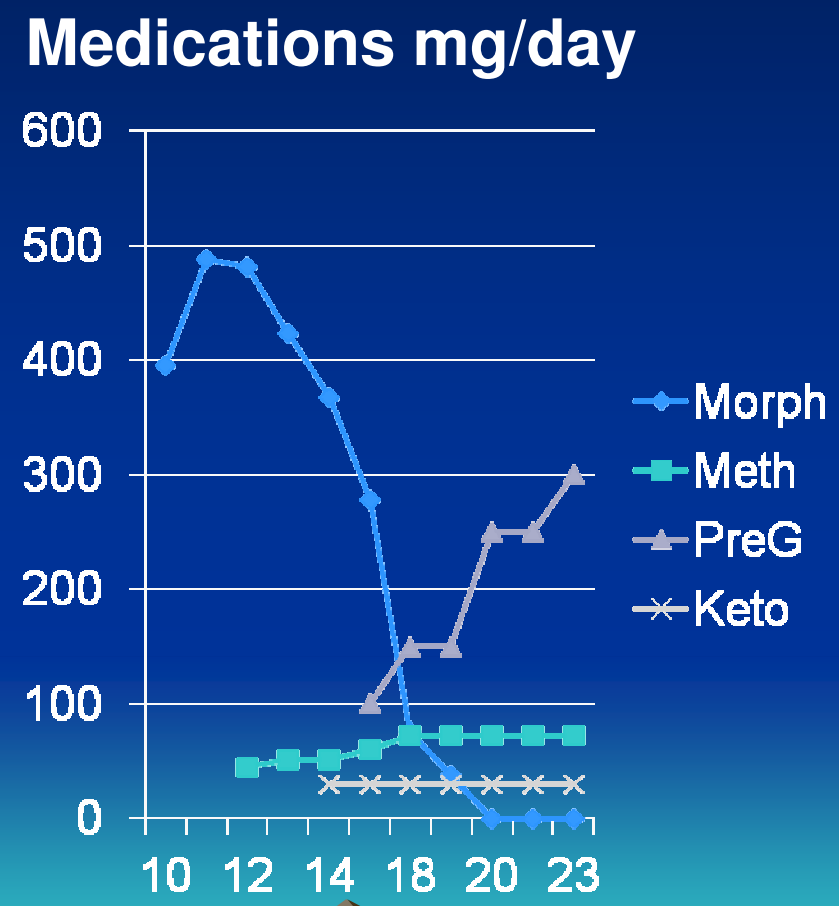
- Jan Feb
  - Oxycodone SR 480 mg, Oxycodone p.r.n. 40 mg Dexamethasone 6 mg, fentanyl TTS 59 ug, pregabalin 50 mg
- 12th Feb RT monofraction
  - Oxycodone p.r.n. reduced stable on other drugs, pain improved
- April
  - Pain recurrence and progression

April

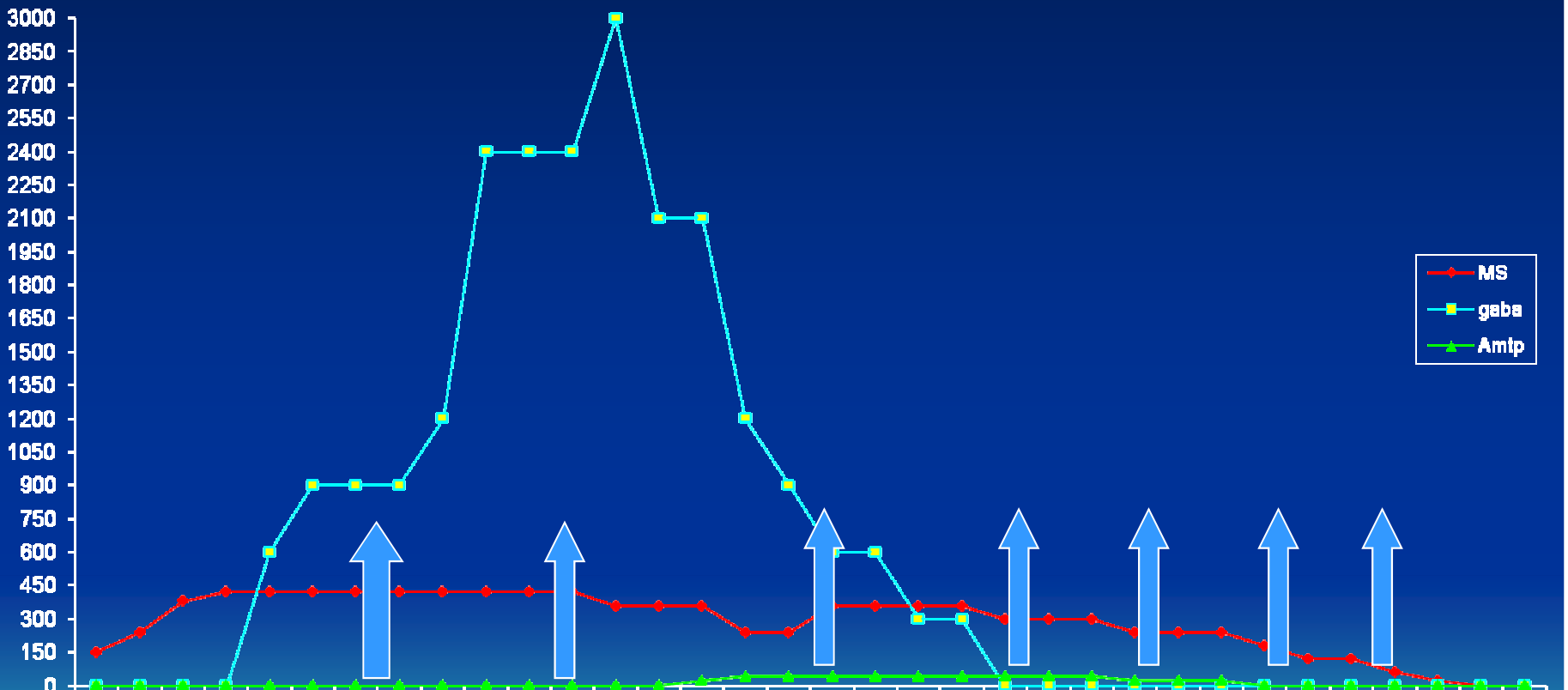
- Pain worsening
- Therapy
  - Oxycodone SR 480
  - Oxycodone IR 200
  - Fentanyl TTS 75 ug
  - Dexamethasone 4 mg

Pain Intensity and Medications





Analgesic regimen during chemotherapy administration (Ewing S.)



	1	2	3	4	5	6	7	8	9	25	26	27	28	35	41	42	43	46	47	48	49	67	68	71	89	90	91	105	114	137 rt	140	158 rt	180	190
MS	150	240	380	420	420	420	420	420	420	420	420	420	360	360	360	240	240	360	360	360	360	300	300	300	240	240	240	180	120	120	60	20	0	0
gaba	0	0	0	0	600	900	900	900	120	240	240	240	300	210	210	120	900	600	600	300	300	0	0	0	0	0	0	0	0	0	0	0	0	0
Amtp	0	0	0	0	0	0	0	0	0	0	0	0	0	0	20	40	40	40	40	40	40	40	40	40	20	20	20	0	0	0	0	0	0	0

Breathlessness

"a subjective experience of
breathing discomfort that consists of qualitatively
distinct sensations that vary in intensity"

American Thoracic Society. Dyspnea. Mechanisms, assessment, and management:
a consensus statement.
American Journal of Respiratory and Critical Care Medicine
1999;159(1):321–40

- Also termed dyspnea, shortness of breath, air hunger, awareness of respiratory distress, or laboured breathing;
- variably perceived by different patients, depending on multiple physiological, psychological, social, environmental, and cultural factors

(Guz A. Brain, breathing and breathlessness. *Respiration Physiology 1997;109(3):197–204*)

Pathophysiology

- Respiratory motor activity is regulated by automatic centres in the brainstem and voluntary signals from the cortex, and controls chest wall expansion, lung inflation, and ventilation. Feedback is provided by chemoreceptors, mechanoreceptors, and sensory receptors;
- breathlessness may be explained by a mismatch between afferent sensory information processed at the cortex and respiratory motor command from the cortex and brainstem.

(Nattie E. Central chemoreceptors. In: Dempsey JA, Pack AL editor(s). *Regulation of Breathing. 2nd Edition. New* York: Marcel Dekker, 1995:473–510; Nishino T. Dyspnoea: underlying mechanisms and treatment. *British Journal of Anaesthesia 2011;106(4):* 463–74)

clinical practice guidelines

Annals of Oncology 26 (Supplement 5): v169–v173, 2015
doi:10.1093/annonc/mdv306

Treatment of dyspnoea in advanced cancer patients: ESMO Clinical Practice Guidelines†

M. Kloke[1] & N. Cherny[2], on behalf of the ESMO Guidelines Committee*

One of the most distressing symptoms in cancer patients; highest prevalence in lung cancer (up to 74%) increasing in the terminal phase (up to 80%)

Assessment

- Completely subjective in perception → the most valid assessment instrument is the patient-reported outcome;
- differentiation between continuous, episodic, breakthrough or crisis breathlessness;
- Evaluation of onset, exacerbating and relieving factors.

Dimension of dyspnea

Dimension	Criterion	Measurement
Sensory-perceptual experience	Intensity	NRS, VAS
Affective distress	Emotional unpleasantness	NRS, VAS, HADS
Impact on daily life	Meaning for social contact, functioning, quality of life	CRQ, EORTC-QLQ-C15-PAL, MRC, SF12

NRS, Numerical Rating Scale; VAS, visual Analogue Scale; MRC, Medical Research Council; CRQ, Chronic Respiratory Disease Questionnaire; HADS, Hospital Depression and Anxiety scale®; SF12 Health survey®; EORTC-QLQ-C15-PAL questionnaire to assess the quality of life of palliative cancer care patients.

M. Kloke, on behalf of the ESMO Guidelines Committee, N. Cherny, on behalf of the ESMO Guidelines Committee; Treatment of dyspnoea in advanced cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol* 2015; 26 (suppl_5): v169-v173. doi: 10.1093/annonc/mdv306

Management strategies

- Treating reversible causes (intervention according pathophysiology)
- Non-pharmacological interventions
- Pharmacological treatment

Treating reversible causes

Pathophysiology	Targeted intervention
Pleural effusion	Pleural drainage, pleurodesis
Cancer-induced airways obstruction	Endoscopic or surgical intervention (stent, laser, argon-beamer) Localised radiotherapy
Anaemia	Transfusions Erythropoietin administration for chemotherapy-induced anaemia
Infections, e.g. pneumonia	Antibiotics, antifungal drugs
Airway obstruction and chronic obstructive pulmonary disease as comorbidity	Airway dilatators, corticosteroids
Haemoptysis	Antifibrinolytics, endoscopic or surgical intervention (stent, laser, argon-beamer), irradiation
Pulmonary congestion	Diuretics or other appropriate intervention
Pericardial effusion	Pericardial puncture, pericardiodesis
Upper venous congestion	Corticosteroids, irradiation, stenting of the vena cava, anticoagulation
Chest pain	Optimised analgesia

M. Kloke, on behalf of the ESMO Guidelines Committee, N. Cherny, on behalf of the ESMO Guidelines Committee; Treatment of dyspnoea in advanced cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol* 2015; 26 (suppl_5): v169-v173. doi: 10.1093/annonc/mdv306

Non-pharmacological interventions

- **Education** of the patient and relatives about simple measures for ameliorating the symptom (i.e cooling the face, opening windows, using small ventilators, adequate positioning, respiratory training);
- **Oxygen**: no evidence that relieves dyspnea, unless the patient suffers from hypoxaemia.

Pharmacological treatment tried

- Cholinesterase inhibitors (theophylline)
- NSAIDs
- Benzodiazepines
- Phenotiazines
- Opioids

Pharmacological treatment

Opioids:

- the only pharmacological agents with sufficient evidence;
- can be used in opioid-naive as well as in opioid-tolerant patients;
- mechanism of the antidyspnoeic effect of opioids is mediated via opioid receptors of the cardio-respiratory system as well as different areas in the central nervous system;

- evidence has been provided only for oral and parenteral morphine, diamorphine and dihydrocodeine;
- subcutaneously and intravenously applied opioids are effective, with the intravenous form having the most rapid onset;
- no evidence for the efficacy of nebulised or inhaled opioids;

- normal-release preparations of oral/rectal opioids may be used for titration, switching to sustained preparation afterwards;
- in opioid-naïve patients the starting dose for dyspnea is smaller than that for pain palliation;
- patients receiving opioids for analgesia require an increase of dosage up to 25% or 50%.

Benzodiazepines:

- can be used in cases of non or insufficient response to opioids, either alone or in addition to opioids, especially in patients experiencing anxiety;

- the impact of muscle relaxation and its potential contribution to the intensification of dyspnea, especially in cancer cachexia and sarcopenia, should be taken into consideration.

Steroids:

- effective in dyspnea caused by lymphangiosis carcinomatosa, radiation pneumonitis, superior vena cava syndrome, an inflammatory component, or in (cancerinduced) obstruction of the airways.

Neuroleptics:

- evidence is lacking and therefore they cannot be recommended.

Antidepressants:

- not yet been proven.

Barnes H, McDonald J, Smallwood N, Manser R.

Opioids for the palliation of refractory breathlessness in adults with advanced disease and terminal illness.

Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD011008. DOI:10.1002/14651858.CD011008.pub2.

Multidisciplinary approach: physical, as well as psychological, social and spiritual domains

An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial

Irene J Higginson, Claudia Bausewein, Charles C Reilly, Wei Gao, Marjolein Gysels, Mendwas Dzingina, Paul McCrone, Sara Booth, Caroline J Jolley, John Moxham

Lancet Respir Med 2014;2:979-87

- Single-blind randomised trial;
- 105 patients with refractory breathlessness (breathlessness that continues once treatment of the underlying disease is optimized);
- advanced disease: cancer, chronic obstructive pulmonary disease (COPD), chronic heart failure, interstitial lung disease, and motor neuron disease;
- three large teaching hospitals and via general practitioners in South London

- Primary outcome:

patient-reported breathlessness mastery → a quality of life domain in the Chronic Respiratory Disease Questionnaire, composite score from four questions on feeling of control over the disease and its effects on quality of life and function.

•Results:

mastery of breathlessness was improved in the intervention group at 6 weeks compared with the control group

- First study reporting a survival advantage with palliative care outside of studies of patients with cancer.
- The breathlessness support service:

Additional service to usual UK National Health Service (NHS) care: multi-professional integrated service that combines respiratory, physiotherapy, occupational therapy, and palliative care assessment and management.

First outpatient clinic appointment with respiratory medicine and palliative care clinicians → agree a crisis plan and receiving a breathlessness pack (information, management, a hand-held fan or water spray, a short mantra to help breathing and relaxation) .

A home assessment 2–3 weeks after the clinic visit done by a physiotherapist and/or occupational therapist

Second and final clinic appointment 4 weeks after the first clinic visit, with a palliative care specialist to agree further actions and a discharge plan