

**MALIGNANT PLEURAL MESOTHELIOMA**  
**PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES**

**Coordinator:**

Jan van Meerbeeck (Thoracic Oncology, MOCA, UZ Antwerpen)

**Authors:**

Jan van Meerbeeck (Thoracic Oncology, MOCA, UZ Antwerpen), Kurt Tournoy (Respiratory Medicine/Thoracic Oncology, OLV-Aalst), Yolande Lievens (Radiation Oncology, UZ Gent), Myriam Rimmelink (Surgical Pathology, Hôpital Erasme ULB), Kristiaan Nackaerts (Pneumology/Respiratory Oncology, UZ Leuven), Philippe Nafteux (Thoracic Surgery, UZ Leuven), Thierry Berghmans (Medical Oncology, Institut Jules Bordet), Paul De Vuyst, (Pneumology, Hôpital Erasme ULB), Paul van Schil (Thoracic Surgery, UZ Antwerpen), Thierry Pieters (Pneumology, Cliniques universitaires Saint-Luc)

**Reviewers:**

Sylvie Lambin (Thoracic Oncology Nurse, Cliniques universitaires Saint-Luc), Marianne Fontaine (Physiotherapist, UZ Leuven), Esther Vandebosch (Psychologist, UZ Leuven), Patricia Eraets (Head Nurse, UZ Leuven), Nathalie Leclercq (Thoracic Oncology Nurse, Institut Jules Bordet), Yves Libert (Psychologist, Institut Jules Bordet), Sarah Houtman (Registered Thoracic Oncology Nurse, OLV Aalst), Ellen Troch (Clinical Psychologist, OLV-Aalst), Sisca Kohl (Oncology Nurse, UZ Antwerpen)

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## PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES

### A. Type of cancer

Mesothelioma of the pleura and the pericard

### B. Short description of the cancer

The crude incident rates of malignant pleural and pericardial mesothelioma (MPM) in Belgium are 2.49 per 100 000 for all cases, 4.15 per 100 000 males and 0.90 per 100 000 females. The mesothelioma incidence has substantially increased over the last 20 years to 273 incident cases in 2011<sup>b</sup>, and will peak around 2020, with an ensuing smooth descending slope, reflecting the persistence of the main carcinogen –asbestos– in the environment. Presenting symptoms of mesothelioma are aspecific: chest pain due to chest wall involvement and/or dyspnoea due to pleural or pericardial effusion, the latter with tamponade of the heart. Although a diagnosis can be suspected on pleural or pericardial fluid cytology, a formal diagnosis and subtyping requires a tissue biopsy, typically obtained via thoracoscopy or transthoracic fine needle biopsy. The disease is considered almost universally fatal. Overall survival is dismal with < 5% of patients alive 5 years after diagnosis and even fewer disease free at that moment. Survival has however, been improving –partly by an earlier diagnosis– and for patients diagnosed in 2005-2009 the one year relative survival estimates were 44.5% in males and 49.5% in females. Whereas complete resection is controversial, a minority of patients (<10%) might benefit from cytoreductive or debulking surgery by either extrapleural pneumonectomy or pleurectomy/decortication as part of a multimodality treatment protocol. Both procedures are complex and require expertise and a dedicated care pathway. MPM is a highly symptomatic cancer and access to specialist palliative interventions will form an important part of any high quality service.

<sup>b</sup>

[http://www.kankerregister.org/default.aspx?url=Statistieken\\_tabellen\\_jaarbasis](http://www.kankerregister.org/default.aspx?url=Statistieken_tabellen_jaarbasis)



### C. Model of care pathway suggested for adult patients with MPM

#### Model of care pathway: A stepped care design

**Step A:** Regional MPM reference centres will be installed, where treatment with radical intent and clinical trials are centralized. Treatment with radical intent includes any attempt at radical resection and/or definitive radiotherapy of the primary tumour, whether or not experimental. At (suspected) diagnosis, all fit patients should be discussed with the specialist mesothelioma multidisciplinary team from the nearest malignant pleural mesothelioma centre in order to select those patients for referral for these treatments.

**Step B:** Radical surgery of any kind will be concentrated in appropriate thoracic surgical reference centres. Although such a surgical reference centre has to be located in a MPM reference centre’s institution, the inverse does not apply; a MPM reference centre should not necessarily qualify as surgical reference centre. In the latter case, MPM and surgical reference centres function however, as close partners; for peri-operative hemi-thorax radiotherapy, e.g. in the context of a treatment with radical intent, the radiation and surgical oncologists partner up in the same MPM centre (see further).

**Step C:** Palliative therapy, including standard palliative chemotherapy or radiotherapy for symptom control, can be done in the peripheral centre, provided that the treatment is coordinated by a multidisciplinary team, including a pulmonologist with oncological competence and/or a medical oncologist, a clinical nurse specialist, a psychologist with a specific training in psycho-oncology and/or in palliative care, a pain specialist, all in close collaboration with primary care and palliative care services.

### D. Phase(s) of the clinical pathway for which Reference Centres are required

	Phase of the Clinical Pathway	MPM Reference Centre	Peripheral Centre
0	Application for compensation to Fund of Occupational Diseases or Asbestos Fund according to Belgian legislation		X
1	MOC (at diagnosis)	X: 2 <sup>nd</sup> opinion MOC	X
2	Diagnostic confirmation	National Mesothelioma Panel	
3a	Diagnostic procedures i.c. thoracoscopy		X
3b	Invasive staging procedures	X	
4a	Treatment with palliative intent, including standard chemotherapy, radiotherapy, pleurodesis		X
4b	Treatment with radical intent, inclusive any attempt of multimodality treatment including extended surgery	X (in collaboration with surgical reference centre)	
4c	Clinical intervention study, for the duration of the trial	X	
5	Follow-up	(x for 4b/4c)	X for 4a
6	At relapse	X: 2 <sup>nd</sup> opinion MOC	



### *Multidisciplinary Oncological Consult (MOC): Peripheral Centre and Reference Centre*

Eligibility for surgery and for clinical trials - with either systemic treatment and/or combined modality- requires a specific knowledge of staging, inclusion and exclusion criteria. This is done as a second opinion-MOC, either by the physical presence of the referring physician at the reference centre's MOC, by teleconsulting (tele-MOC) or after viewing the patient at a specialised consultation in the reference centre.

### *Diagnostic confirmation: Reference Panel*

European guidelines<sup>c</sup> : An independent expert panel should be asked to confirm the diagnosis particularly in clinical trials, or in any case where there is doubt about the diagnosis.

Belgian regulation: National pathology panel review required for compensation by Asbestos Fund or Occupational Diseases Fund

### *Comprehensive anatomico-pathological diagnosis*

The diagnostic procedures leading to a diagnosis of MPM should be available and possible in every general hospital. It is noted that preference should be given to a histological diagnosis. Invasive staging in case of treatment with radical intent (e.g. mediastinoscopy or laparoscopy) should be done in the Reference Centre. Endoscopic Ultrasound (EBUS/EUS) can be performed in a Peripheral Centre, provided it is performed by an experienced pulmonologist and cytology is reviewed .

### *Therapeutic modalities: Reference Centre*

European guidelines<sup>d</sup> advocate to perform:

- extended surgery only in selected patients by experienced thoracic surgeons in the context of a multidisciplinary team and preferably as part of a clinical trial of multimodality treatment;
- postoperative Intensity Modulated thoracic Radiotherapy (IMRT) in specialised centres only;
- clinical trials in mesothelioma by multidisciplinary teams with a profound knowledge of staging and response evaluation;

It was felt by the experts that extended resections in mesothelioma are not the remit of surgical departments without extensive thoracic surgical expertise.

### *Follow-up: Reference Centre*

Only for those patients qualifying for treatment with radical intent (late toxicity) or for the duration of clinical trials.

At relapse, fit patients should be presented at the MOC of the MPM Reference Centre in order to select and refer for participation in clinical trials. Eligibility for clinical trials requires a specific knowledge of inclusion and exclusion criteria. This is done as a second opinion-MOC, either by the physical presence of the

<sup>c</sup> Scherpereel A, Astoul P, Baas P, Berghmans T, Clayton H, de Vuyst P, et al. Guidelines of the European Respiratory Society and the European Society of Thoracic Surgeons for the management of malignant pleural mesothelioma. Eur Respir J 2010; 35: 479–95

<sup>d</sup> Stahel RA, Weder W, Lievens Y, Felip E. On behalf of the ESMO Guidelines Working Group. Malignant pleural mesothelioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2010; 1 (Supplement 5): v126–a8



referring physician at the reference centre's MOC, by tele-consulting (tele-MOC) or after viewing the patient at a specialised consultation in the reference centre.

## E. General and specific minimal criteria for Reference Centres

### *Human Resources and dedicated team*

Specialized staff: members of the specialist mesothelioma multidisciplinary team include the same range of professionals as the lung cancer multidisciplinary team. Each of the following specialities should be represented by at least 1 member:

- Pulmonologist with oncological competence and/or a medical oncologist with a special expertise in mesothelioma, taking managerial responsibility for the service as a whole;
- Thoracic surgeon with experience in the management of pleural disease including mesothelioma, working within the mesothelioma Reference Centre or in a partnered up thoracic surgical unit (see further);
- Radiation Oncologist with a special interest in thoracic oncology and experience in mesothelioma, working within the mesothelioma Reference Centre or in a partnered up radiotherapy department;
- Pathologist with experience in mesothelioma diagnosis;
- Nuclear medicine physician with expertise in thoracic oncology;
- Radiologist with thoracic expertise;
- A clinical nurse specialist, linked to the National Cancer Plan programme, with specialised knowledge of lung cancer and mesothelioma;
- Pain specialist with close links with the palliative care team.

### Multidisciplinary management

- All new 'fit' patients are routinely presented at a specialized thoracic oncology MOC;
- Results of MOC are documented according to the standard requirements of the oncology care programme and Cancer Registry;
- Patients have access to a psychologist with a specific training in the psycho-oncology field, and provided through the oncology care program. If necessary a (liaison) psychiatrist can be consulted;
- Patients have access to dieticians, physiotherapists, social workers, provided through the oncology care programme;
- Adequate and sufficient support to provide the administrative coordination of the multidisciplinary team and the registration of outcome data and provided through the oncology care programme.

Appropriate funding for keeping database and personnel to collect and send quality indicators and required treatment information to the Belgian Cancer Registry



### *Required facilities and equipment*

- Adequate meetings of the National Mesothelioma Panel require an appropriate facility for tele-pathology for participants;
- Surgery: a thoracic surgery reference department is defined as proposed by the Belgian criteria for coordinating training centres in thoracic surgery<sup>e</sup>, either in house or partnered up to the MPM reference centre. A formal collaboration between thoracic surgeon and radiation oncologist is required with regard to postoperative radiotherapy planning;
- Radiotherapy:
  - o planning systems that allow image fusion of different data sets as well as advanced dose computation algorithms (type B algorithms);
  - o linear accelerators at least capable of Intensity Modulated Radio Therapy (IMRT) and Image Guided Radiotherapy (IGRT) (volumetric imaging, cone-beam CT scan);<sup>f</sup>
  - o motion management techniques are highly advisable.
- Chemotherapy is carried out by appropriate specialists and is compliant with local and national quality assurance regulations for chemotherapy administration and acute oncology;
- Imaging: all appropriate imaging inclusive dedicated PET-CT facility and image-guided biopsy modalities are available to patients in a timely manner;
- Laboratory for pathology has access to a range of appropriate immune-histochemical stainings;
- Specialist palliative care including treatment of refractory pain and dyspnoea;
- Dedicated MOC-room with simultaneous projection of imaging and patient data and optional tele-MOC facilities;
- Access to tumour bank;
- Access to an oncological rehabilitation programme;
- Facilities for clinical trial conduct and support, including research nurse and data manager involved in oncology trials according to existing standards (International Conference on Harmonisation Good Clinical Practice (ICH-GCP)).

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<sup>e</sup> See addendum A

<sup>f</sup> IMRT is a high precision form of radiotherapy. It conforms the shape and dose of the radiation precisely to the volume of tumour tissue that needs to be treated; Image Guided Radiotherapy (IGRT) is any imaging at pre-treatment and delivery, the result of which is acted upon, that improves or verifies the accuracy of radiotherapy. IGRT encompasses the whole range from simple visual field alignment checks, through to the more complex volumetric imaging that allows direct visualization of the target volume and surrounding anatomy.





### *Patient centred care*

- Presence of comprehensive institutional Standard Operating Procedures detailing diagnostic, therapeutic management, continuity of care and follow-up of (suspected) mesothelioma patients;
- Core services cover continuity of care 24/7 by specialised staff in agreement with the reference centre's emergency department and house duty call rules. This applies for services provided by the departments of pulmonology, thoracic surgery, radiology, oncology and pain specialist;
- Support services for the patient are available through the Oncology care programme;
- National and international networking with other national and international Reference Centres for second opinion or specific indications which require further centralisation of expertise, e.g. cordotomy, pleural IMRT, experimental targeted treatment, referral to phase 1 clinical trials;
- Tele-MOC facilities with other hospitals and specialists in order to discuss eligibility for referral.

### *Minimal volume of patients*

- For MPM reference centres: after a run-in period of 5 years, an average caseload of at least 20 patients with mesothelioma per year, referred for either diagnosis, treatment or second opinion. Less than half of these should consist of second opinions, referred without further treatment in the reference centre.
- For surgical reference centres: as radical surgery is not a standard therapeutic approach for MPM, it is impossible to propose a minimal number of patients defining a reference surgery centre for radical mesothelioma surgery. Up to 10% of MPM patients are expected to receive radical surgery treatment, which corresponds to  $\pm 30$  patients /year in Belgium<sup>9</sup>. We propose that a surgical reference centre for radical/ extended mesothelioma surgery is defined as a coordinating training centre for thoracic surgery (as defined by the Belgicum Collegium Chirurgicum (addendum A)) and is handling - after a run-in period of 5 years - at least 5 patients per year by any kind of radical surgery. In case a surgeon trained in such a reference surgery centre aims to develop a programme for radical MPM surgery in another MPM reference centre, the same criteria have to be fulfilled to consider the reference centre as a new reference surgical centre.

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<sup>9</sup> Damhuis R, Khakwani A, de Schutter H, van Meerbeeck J, Rich A, Burgers J. International comparison of treatment and survival for pleural mesothelioma, combined analysis of 9.014 patients from Belgium, the Netherlands and England. In press



*Quality Assurance*

- Diagnosis of the local pathologist should be confirmed within reasonable delay (< 2 weeks) by the specialist mesothelioma panel of pathologists. This frequency of meetings will require the financing of the installation of tele-pathology (see above).
- Annual activity report on number of new patients, diagnostic, treatment and outcome data.
- Capacity to propose quality indicators (structure, process, outcomes)
  - o Structure indicator: composition of the multidisciplinary team and technical determinants of the centre
  - o Process indicators
 

	Threshold
1. fraction of referred patients seen within 2 weeks of referral	95%
2. fraction of referred patients discussed at MOC of Reference Centre	100%
3. fraction of patients starting tumour directed treatment within 1 month after the MOC where the therapeutic decision was proposed	85%
- Outcome indicators
 

4. 30-day mortality of radical surgery (average on a 3 year base)	<7%
90-day mortality of radical surgery (average on a 3 year base)	<15%
5. 1-year and 5-year survival rate (to be provided by the Belgian Cancer Registry)	

*Research and other scientific activities*

- Participation to clinical trials in which patients with mesothelioma can be recruited, including local, national and international, observational, translational and interventional studies of any phase
- Medical team members versed in clinical management of patients have proficiency in mesothelioma care and in clinical trial conduct (GCP accreditation)
- Link with a tumour bank
- Quality indicators
  - o fraction of referred patients are enrolled in a study over a period of 3 years 10%
  - o fraction of operated patients having their tissue banked and linked with clinical data 80%



### *Educational activities: Teaching and dissemination*

- Involvement in training and continuous education programmes (annual or multi-annual training / educational programme for physicians, nurses, supportive disciplines) is encouraged.
- Organisation / communication in scientific congresses
- Organisational strategy to prevent burn-out or emotional fatigue and care for moral distress in caregivers (e.g. through meetings, intervision, training, coaching, ...)

### **Additional comments**

1. As expertise is linked to experts, Reference Centres should be audited every 5 years for their performance based on the proposed quality indicators.
2. As knowledge about mesothelioma is rapidly evolving, the criteria for Reference Centres should be re-evaluated at least every 5 years, preferably with the aid of the KCE.
3. The instalment of Reference Centres for mesothelioma is conditional of the official recognition procedure of the titles of pulmonologist with oncological competence<sup>h</sup> and of general surgeon with thoracic surgical competence.
4. Care should be taken that the financing of the Reference Centres is appropriate and takes into account the multitude of extra tasks required.

### **Addendum A: Minimal criteria to fulfill to be recognized as Coordinating Training Centre for Thoracic Surgery, as proposed by the Belgicum Collegium Chirurgicum**

1. A centre dealing with all fields of General Thoracic Surgery, including Thoracic Oncology.
2. At least 75 major thoracic surgery operations per year should be performed in the centre.
3. At least two staff surgeons should be appointed full time in the centre, both bearing the title of Specific Competence in Thoracic Surgery and dedicating at least 50% of their activities to General Thoracic Surgery. One staff surgeon should have the degree of surgery for at least 8 years, the second for at least five years.
4. The centre should be held responsible for keeping records and patients files according to the at the moment accepted quality norms.
5. The centre should be responsible for the organization of training programs in Thoracic Surgery.
6. At least every 3 months, staff meeting for medical and paramedical staff should be organized.
7. Internal quality controls should be organized.

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<sup>h</sup> Federale Overheidsdienst Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu. Ministerieel besluit tot vaststelling van de bijzondere criteria voor de erkenning van geneesheren-specialisten, houders van de bijzondere beroepstitel in de medische oncologie en van de bijzondere beroepsbekwaamheid in de oncologie evenals van stagemeesters en stagediensten voor deze disciplines en deze bijzondere beroepsbekwaamheid. Belgisch Staatsblad N. 2007 — 2308 [C – 2007/22836]/ Service Public fédéral Santé Publique, Sécurité de la Chaîne alimentaire et Environnement. Arrêté ministériel fixant les critères spéciaux d'agrégation des médecins spécialistes porteurs du titre professionnel particulier en oncologie médicale et de la qualification professionnelle particulière en oncologie ainsi que des maîtres de stage et des services de stage pour cette spécialité et cette qualification professionnelle particulière. Moniteur Belge N. 2007 — 2308 [C – 2007/22836].