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‘The Melorheostosis module: a collaboration between ECTS, ERN BOND and EuRREB’

EuRREB
European Registries for Rare
Endocrine and Bone conditions

The Melorheostosis module a collaboration between ECTS - ERN BOND and EuRREB

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EuRREB
European Registries for Rare Endocrine and Bone conditions

Université de Paris

Inserm

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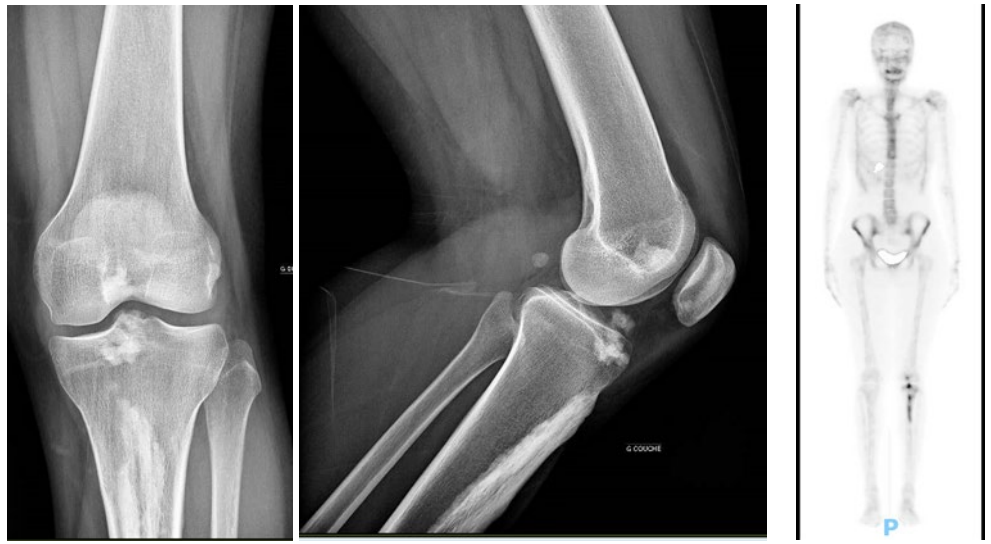
Melorheostosis

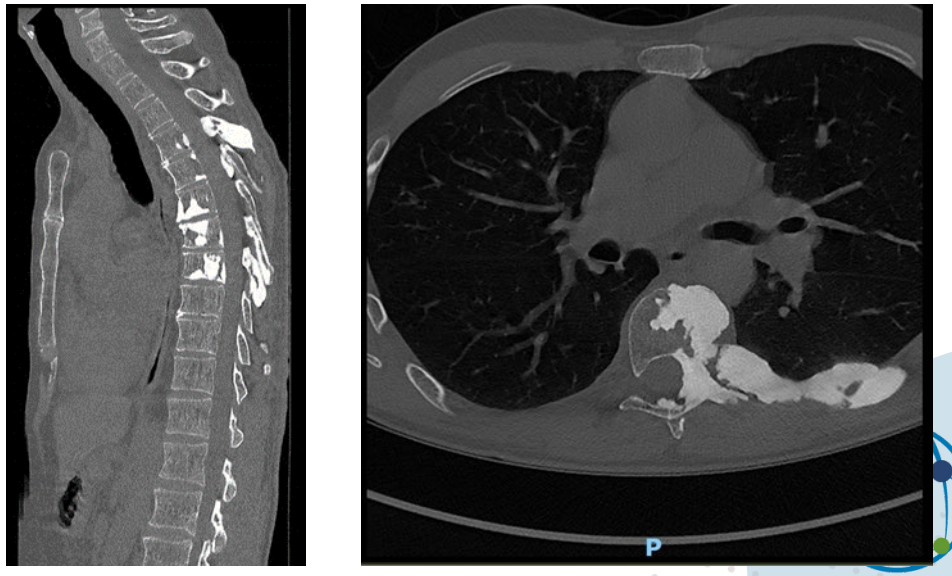
Sclerosing bone dysplasia

Revealed by X-rays in late adolescence or early adulthood
Affects the lower extremities of long bones
Limited to one side of the body, also other bones.

Deformities, stiffness, joint contractures
skin changes and vascular involvement
Pain

Biopsy rarely performed although useful for differential diagnosis.





Melorheostosis

Estimated prevalence is 1/1,100,000

- **400 cases reported in literature**
- **Most of published are case series, include approximately 20 patients (range 19–24 years).**

Natural course unknown, long-term data are lacking.

No guidelines addressing the management of patients

No specific treatment available

Initial dataset : ECTS - ERN Bond initiative 2022

ECTS
European Calcified Tissue Society

ERN BOND
EUROPEAN REFERENCE NETWORK
ON RARE BONE DISEASES

HCP	PATIENT ID	FAMILY ID	PROBAND	PERSONAL INFORMATION		PATIENT STATUS		DISEASE HISTORY				DIAGNOSIS OF RARE DISEASE (ORPHA CODE)
				DATE OF BIRTH	SEX	STATUS	DATE OF DEATH	AGE/PERIOD AT ONSET	AGE AT DIAGNOSIS	DATE AT DIAGNOSIS	FAMILY HISTORY	
			Yes	dd/mm/yyy	Female	Alive	dd/mm/yyyy	Years (in number)	Years (in number)	dd/mm/yyyy	Negative	1306: Buschke-Ollendorff syndrome
			No	Foetus	Male	Dead		Antenatal	Antenatal		Positive - Maternal	1879: Melorheostosis with osteopoikilosis
				Unknown	Unknown	Lost in follow-up		Neonatal (0-4 weeks)	Neonatal (0-4 weeks)		Positive - Paternal	2485: Melorheostosis
								Infancy (4 weeks-23 months)	Infancy (4 weeks-23 months)		Positive - Unknown	166119: Isolated osteopoikilosis
								Childhood (2-11 years)	Childhood (2-11 years)		Unknown	
								Adolescent (12-18 years)	Adolescent (12-18 years)			
								Adult (≥ 19 years)	Adult (≥ 19 years)			

Initial dataset

CLINICAL FEATURES																				
DATE AT VISIT	AGE AT VISIT	HEIGHT (m)	WEIGHT (kg)	BMI	X-RAY FEATURES	HYPEROSTOSIS	INVOLVED SITE	SKELETAL DYSPLASIA (DEFORMITY)	JOINT STIFFNESS	ASYMMETRY	JOINT LIMITATION	SWELLING	PAIN	PAIN - ADULT (VAS scale)	PAIN - CHILD (3-8 Y) (Wong-Baker FACES scale)	SITE INVOLVED BY PAIN	MUSCLE ATROPHY	ABNORMALITY OF THE SKIN	SKIN ABNORMALITY DETAILES	VASCULAR ABNORMALITIES
dd/mm/yyyy	Years (in number)	1,76	70,00	22,6	No bone lesions	No		No	No	Lower Limbs	No	No	No	0	0		No	No		No
					Buschke-Ollendorff syndrome	Yes		Yes - Left Lower Limb	Yes	Upper Limbs	Yes - Left Lower Limb	Yes - Left Lower Limb	Yes	1	2		Yes	Yes		Yes
					Melorheostosis with osteopoikilosis	Not evaluated		Yes - Right Lower Limb	Not evaluated	Both	Yes - Right Lower Limb	Yes - Right Lower Limb	Not evaluated	2	4		Not evaluated	Not evaluated		Not evaluated
					Melorheostosis			Yes - Lower Limbs		None	Yes - Lower Limbs	Yes - Lower Limbs		3	6					
					Isolated osteopoikilosis			Yes - Left Upper Limb			Yes - Left Upper Limb	Yes - Left Upper Limb		4	8					
								Yes - Right Upper Limb			Yes - Right Upper Limb	Yes - Right Upper Limb		5	10					
								Yes - Upper Limbs			Yes - Upper Limbs	Yes - Upper Limbs		6						
								Not evaluated			Not evaluated	Not evaluated		7						
														8						
														9						
														10						

GENETIC ANALYSIS GERMINAL					GENETIC ANALYSIS SOMATIC					RESEARCH				
GENETIC DIAGNOSIS - GERMINAL (HGNC:28887 LEMD3)	EXON	DNA c.	PROTEIN p.	MUTATION TYPE	GENETIC DIAGNOSIS - SOMATIC (HGNC:28887 LEMD3)	EXON	DNA c.	PROTEIN p.	MUTATION TYPE	CONSENT	SAMPLE AVAILABILITY	TYPE OF SAMPLE (OBIB CODE)	LINK TO BIOBANK	LINK
Wild type				Big del	Wild type				Big del	No	No	Blood	No	https://directory.bbmri-eric.eu
Mutation				Big dup	Mutation				Big dup	Yes	Yes	DNA	Yes	
Not performed				Frameshift	Not performed				Frameshift			Saliva		
				Inframe del-ins					Inframe del-ins			Tissue		
				Missense					Missense					
				Nonsense					Nonsense					
				Splicesite					Splicesite					
				No Mutation					No Mutation					
				Not performed					Not performed					

Strategy

ECTS database:

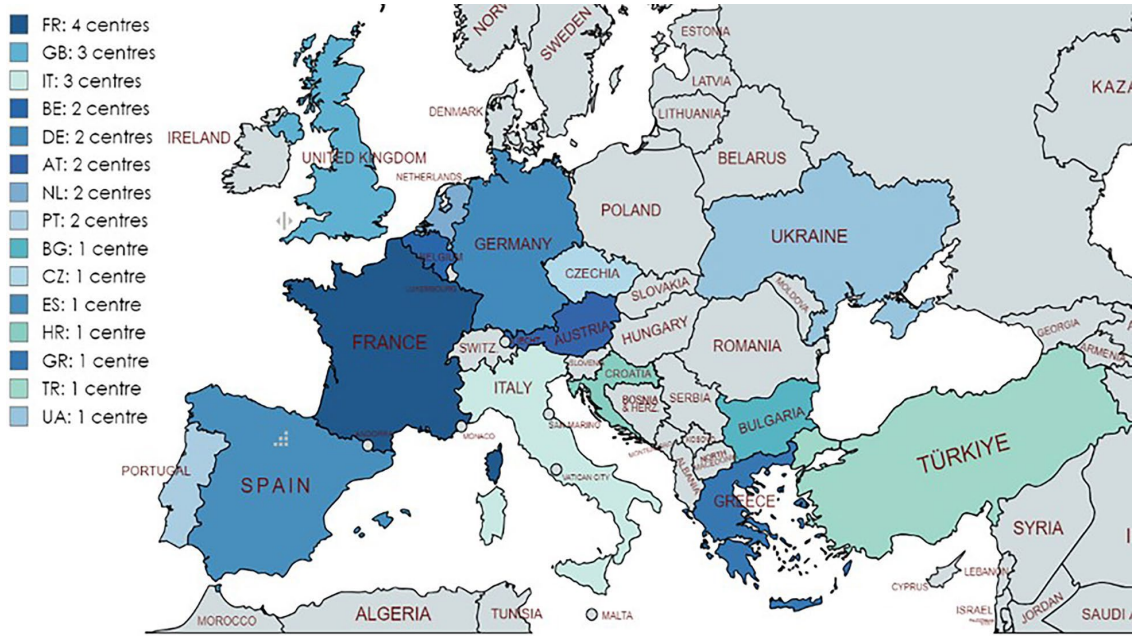
- No available platform for the collection
- Regulatory limitations accross EU
- Financial support

⟶ Develop a standard dataset in the European registries for rare endocrine and bone conditions

EuRREB

2 registries:

- **e-REC:** an electronic-REporting of conditions platform that collect monthly number of new cases based on ORPHA codes and to support the continuous monitoring program of the ERNs.
- **Core registry**



Achondroplasia data dictionary (Download, 43 KB) **Recently updated!**
Fibrous Dysplasia / McCune Albright Syndrome (FD/MAS) data dictionary (Download, 59 KB)
Gender Incongruence data dictionary (Download, 30 KB)
iPPSD/PHP data dictionary (Download, 86 KB)
Langerhans Cell Histiocytosis (LCH) data dictionary (Download, 20 KB) **NEW!**
Melorheostosis data dictionary (Download, 52 KB)
Non-Langerhans Cell Histiocytosis data dictionary (Download, 19 KB) **NEW!**
Osteogenesis Imperfecta (OI) data dictionary (Download, 63 KB)
Parathyroid Carcinoma data dictionary (Download, 172 KB)
Pediatric Differentiated Thyroid Carcinoma data dictionary (Download, 59 KB)
Pituitary Tumour data dictionary (Download, 30 KB)
Rare Hypophosphataemia data dictionary (Download, 69 KB)
Rare Obesity data dictionary (Download, 38 KB)

Dictionaries (https://eurreb.eu/registries/data-dictionaries/).

Development of a dictionary

Centre
Country
Register ID
Consent for registry
Date of Birth
Condition Group
Pseudonymised ID
Sex at birth
Current gender
Country at birth
Country of usual residence
Patient follow-up status
Date of Death
Primary cause of Death
Can be contacted for research purposes by a clinician responsible for patient
Data can be shared for research purposes
Can be contacted for collecting patient reported outcomes

Consent for Newsletters
e-REC ID
First Contact with Centre
Clinician Responsible for Patient
Date of First Clinical Manifestations
How was Diagnosis Reached
Date of Diagnosis
Primary Endocrine Condition
Specific Diagnosis
Participation in Detailed Disease Registry
Detailed Disease Registry
Detailed Disease Registry ID
Biobank Sample Available for Research
Biobank Details
Biobank Patient ID

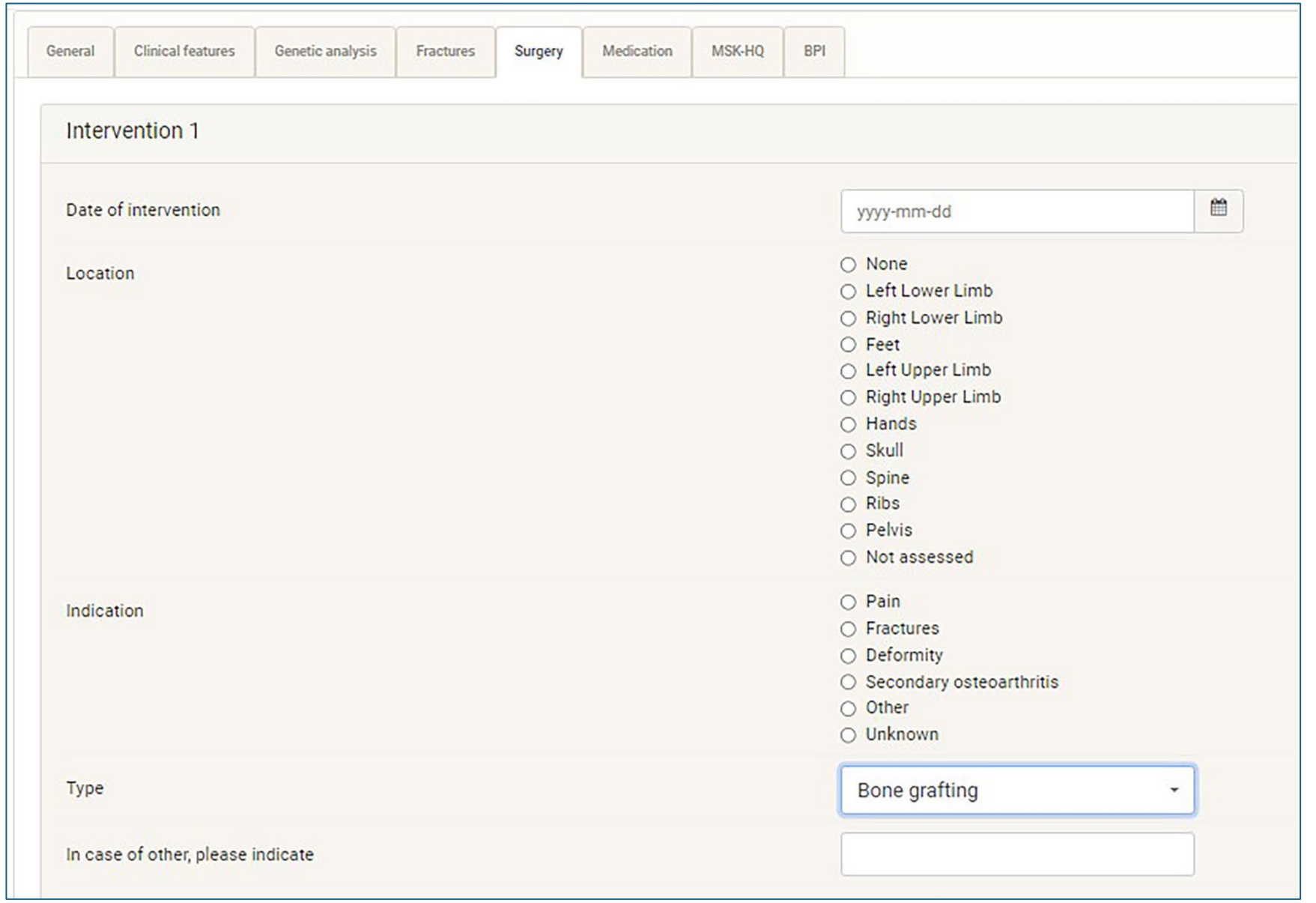
Specific modules

- Proband
- Family and Family history
- Height / Weight / BMI
- X-Ray features : No bone lesions, Buschke-Ollendorff syndrome, Melorheostosis with osteopoikilosis, Melorheostosis, Isolated osteopoikilosis with Orphacode
- Hyperostosis : Involved site (lower Limb, upper limb, hand, foot, vertebrae)
- Deformity: involved site (lower Limb, upper limb, hand, foot, vertebrae)
- Joint: Stiffness, limitations, swelling
- Muscle atrophy
- Skin lesions
- Vascular lesions
- Fracture: site, surgery (type and device)
- Medications: duration and side effects

Pain: site, VAS, for children (Wong-Baker FACES scale)
Quality of life
Mobility score

Genetic diagnosis – germinal or somatic (mutations)

Exemple of melorheostosis module on the Core registry platform



Results

15 patients
13 women
Age at diagnosis : 37± 14 years

Clinical and radiological findings		Number of patients, n (%)
Females		15 (83.3%)
Affected site	Lower limbs	12 (**66.7%**)
	Upper limbs	1 (5.5%)
	Lower leg	11 (61.1%)
	Feet	2 (11.1%)
	Spine	2 (**11.1%**)
	Ribs	2 (**11.1%**)
	Skull	1 (5.5%)
	Pelvis	1 (5.5%)

More than 1 lesion present	**2 (11.1%)**
Pain	14 (**77.8%**)
Hyperostosis	3 (16.7%),
Skeletal deformity	6 (**33.3%**)
Joint stiffness	11 (**61%**)
Joint limitation	12 (**66.7%**)
Asymmetry	16 (88.9%)
Swelling	1 (5.5%)
Muscle atrophy	1 (5.5%)
Vascular abnormalities	1 (5.5%)
Skin abnormality	1 (5.5%)

Limitations and future perspectives

Biases :
Data are collected in the most symptomatic patients as referred to specialist centres
Asymptomatic or minimally symptomatic patients may not be captured
Accurate prevalence ?

Improvements:
Being more systematic in the evaluation of pain
Assess the cause of joint stiffness and reduced mobility
Evaluate the quality of life through questionnaires

Thank you

Ways to contact us:

eurreb.eu

registries@lumc.nl

drop-in sessions via Zoom

European Registries for Rare Endocrine and Bone Conditions

EuRREB
European Registries for Rare
Endocrine and Bone conditions

Endo-ERN
European Reference Network on Rare Endocrine Conditions

ERN BOND
EUROPEAN REFERENCE NETWORK ON RARE BONE DISEASES