Can MR-guided high intensity focused ultrasound (MRgHIFU) replace palliative radiotherapy in the treatment of painful bone metastases?

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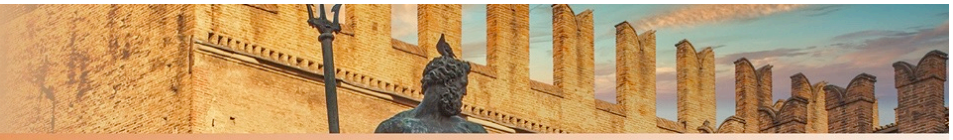


- Cancer induced bone pain strongly interferes with quality of life and daily functioning of cancer patients

(Mantyh PW et al. Bone cancer pain: from mechanism to therapy. Curr Opin Support Palliat Care 2014)

- For patients with bone metastases, it is crucial to provide fast and sufficient pain relief to optimize QoL

(Ripamonti C et al. Malignant bone pain: pathophysiology and treatments. Curr Rev Pain 2000)

- The current standard of care for pain palliation includes EBRT

(Chow E et al. Update of the international consensus on palliative radiotherapy endpoints for future clinical trials in bone metastases. Int J Radiat Oncol Biol Phys 2012)

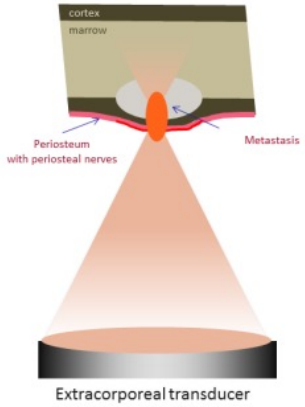
- Usually takes a few weeks to induce adequate pain relief; 30–40% of patients show no response and approximately 50% of the responders experience recurrent pain

(van der Velden JM et al. Evaluation of effectiveness of palliative radiotherapy for bone metastases: a prospective cohort study. J Radiat Oncol 2018)
(Huisman M et al. Effectiveness of reirradiation for painful bone metastases: a systematic review and meta-analysis. Int J Radiat Oncol Biol Phys 2012)

- Magnetic Resonance image-guided High-Intensity Focused Ultrasound (MRgHIFU), as an alternative or in addition to EBRT, may improve pain palliation in these pts by increasing the percentage of responders and decreasing the time to response

(Catane R et al. MR-guided focused ultrasound surgery for the palliation of pain in patients with bone metastases—preliminary clinical experience. Ann Oncol 2007)
(Napoli A et al.Primary pain palliation and local tumor control in bone metastases treated with magnetic resonance-guided focused ultrasound. Invest Radiol 2013)

BUT



Large datasets on the feasibility of MRgHIFU are not available and therefore the rate of pts who can benefit from this therapy is unclear

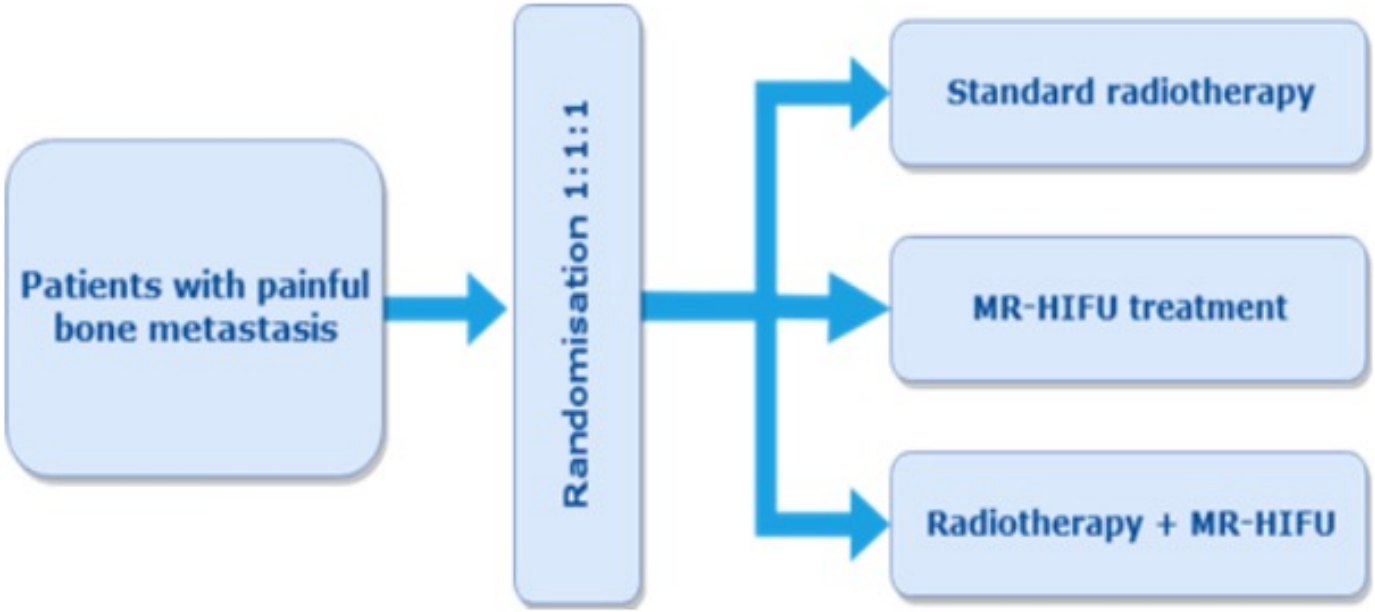
- to report the preliminary results of screened patients in a radiotherapy center for inclusion in a randomized study of MRgHIFU versus EBRT versus MRgHIFU plus EBRT (The FURTHER-trial, H2020)

FURTHER

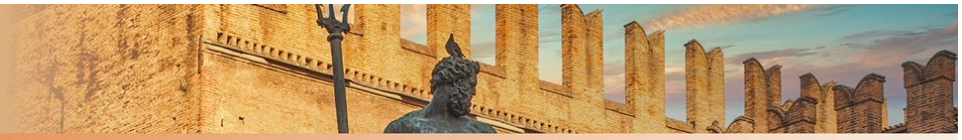
Focused Ultrasound and RadioTHERapy for Noninvasive Palliative Pain Treatment in Patients with Bone Metastases

- Prospective
- Multicenter
- three-armed randomized controlled trial
- performed in six hospitals in four European countries

HORIZON 2020



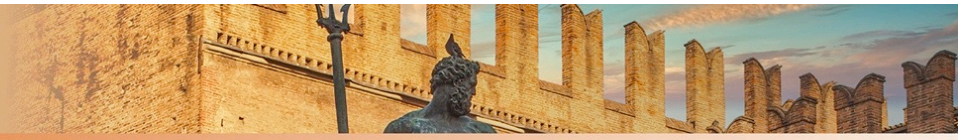
Single or multiple fraction EBRT or SBRT



Inclusion criteria	Source
Age ≥ 18 years	Birth date
Patient capable of giving informed consent	Physician's interview
Referral to radiotherapy department due to painful metastatic bone lesion (NRS ≥ 4)	Referral letter
Pain from target lesion is distinguishable from other lesions *	Physician's interview
Target lesion location is accessible for MR-HIFU and EBRT **	Radiology
Target lesion is visible on pre-treatment MR or CT imaging, with a maximum diameter of 8 cm	Radiology
Participant able to fit in the MRI gantry	Physician's examination
Reasonable performance score (KPS ≥ 50% or Zubrod/ECOG/WHO < 3)	Physician's interview
Life expectancy ≥ 3 months	Referral letter

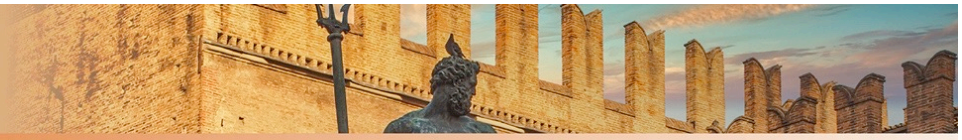
** Solitary painful metastatic bone lesion or multiple metastatic lesions with one predominantly painful target lesion (≥2 points higher pain score than other lesions).*

*** e.g.: Extremities, pelvis (os pubis, os ilium, os ischium, sacrum, acetabulum), shoulders, in selected cases ribs and sternum (if no lung tissue in HIFU beam path)*



Exclusion criteria	Source
Previous surgery on the target location	Patient history
Neurological symptoms due to nerve involvement of target lesion	Physician's examination
Need for surgery of targeted location due to (impending) pathological fracture	Referral letter
Unavoidable critical structures or dense tissues in target area *	Radiology
Curative intention of treatment plan	Referral letter
Contra indications MRI or sedation	Physician's interview
Participant enrolled in another clinical interventional study related to bone metastases treatment or pain relief treatment	Physician's interview
Clinically relevant medical history or physical findings that could interfere with the patient's safety as judged by the treating physician	Physician's interview

** as judged by the operator. e.g.: nerve bundles, skin, extensive scarring, non-targeted bones, air (e.g. hollow viscera), (external) fixation device*



Primary outcome

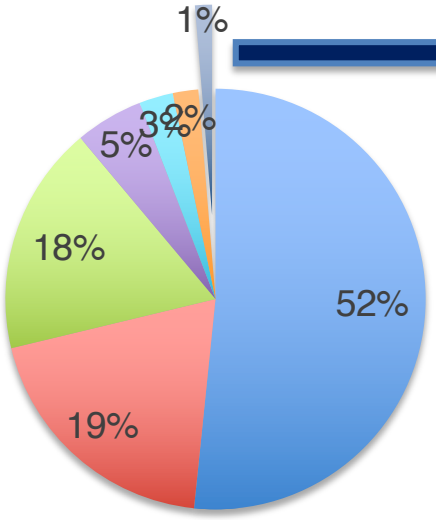
pain response at 14 days after completion of the treatment

Secondary outcomes

pain response at 14 days after inclusion
pain scores
toxicity
adverse events
QoL
survival in the first 6 months after treatment
cost-effectiveness of the treatments

SCREENED PATIENTS (n=153)

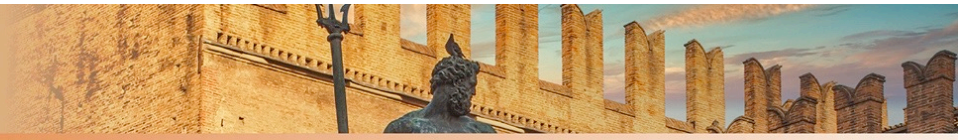
February 2021-June 2022



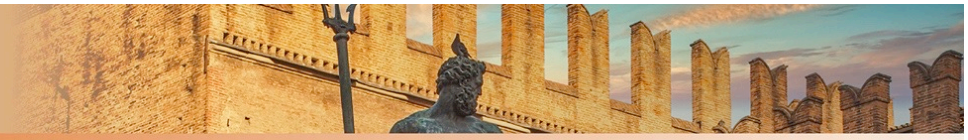
1% ENROLLED PATIENTS

99% EXCLUDED PATIENTS

- spine or skull lesions (51.6%)
- NRS 0-3/non-distinguishable pain (19.6%)
- target non-aceesible or MRI controindicattions (17.6%)
- previous surgery or pathological fractures (5.2%)
- KPS < 50% (2.6%)
- curative intent of EBRT (2.0%)



- MRgHIFU is a promising modality of palliation in pain from bone metastases, especially in pts with symptoms resistant to EBRT.
- The results of our analysis show that the percentage of pts enrolled in a MRgHIFU trial is only 1%, with about 75% of pts excluded due to intrinsic limitations of this therapy
- The implementation of this technique could be justified only in a few centers with a high degree of expertise.



Thank you
for your attention