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Site – Specific Skeletal Dosimetry: From Mean Absorbed Dose to Absorbed Dose Distribution.

M. Lyra, G. Papanikolos, G.S.Limouris

Radiation Physics Unit, A'Department of Radiology
University of Athens, Greece (Hellas)

Optimum therapeutic management of patients suffering from metastatic bone pain, requires accurate calculations concerning absorbed doses.

- Mean absorbed dose, which is the current parameter used to predict the efficacy of the treatment, can either overestimate or underestimate, not only actual dose delivered by these organs/tissues of interest but biological effect as well.

- This study attempts to present more revealing parameters concerning the efficiency of therapeutic schemes with Re-186HEDP and Sm-153EDTMP, such as dose distributions and time – dose rate curves

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PHYSICAL PROPERTIES OF Sm-153

- $T_{1/2}$ = 46,3 h

- Beta energies:
  - 810 keV (20%)
  - 710 keV (49%)
  - 640 keV (30%)

High dose rate

Regions of high osteoblastic activity

Reduced residual activity in bone marrow

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PHYSICAL PROPERTIES OF Re – 186

- $T_{1/2}$ = 3.77 days
- Beta – energies:
- → Emax,1=1.077 MeV (71%)
- → Emax,2=0,939 MeV (22%)
- Maximum range in tissue: 0.48 cm
- Gamma emission: 137 keV (9%)

- High doses in areas of concentration
- Relatively high dose rates for a short time
- Sparing adjacent tissues
- Possible re – treatment

- Scintigraphic imaging during therapy
- Biodistribution estimation for patient – specific dosimetry calculations

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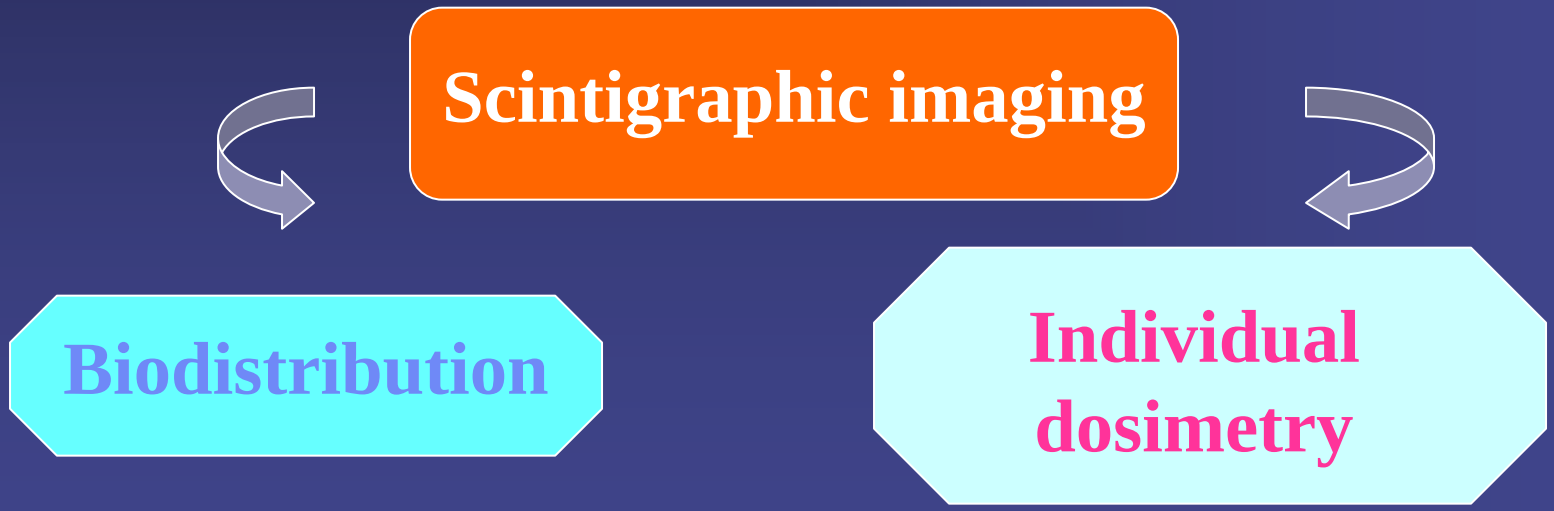
Sm-153-EDTMP Re-186-HEDP

Gamma photon energy:

Sm-153: 103 keV (28%) Re-186:137 keV (9%)



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Use of Sm-153-EDTMP for palliative therapy of bone metastases

- Significant pain relief (at 75% of patients)
- Results appear shortly after 1st administration (1 week)
- Lasting results (up to 16 weeks)
- Multiple administrations possible
- Minimum toxicity effects

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BIOKINETICS OF 186Re – HEDP

What does HEDP stand for?

1,1 – **H**ydroxy**E**thylidene **D**iphos**P**honate

- It is a pyrophosphate analogue
- It offers selective localization in osteoblastic skeletal metastases by bridging the hydroxyapatite crystals
- It follows a biokinetic model consisting of 3 basic compartments:
- Skeleton, Soft – tissue, Urinary excretion

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Measurements of bone uptake are completed by

- using gamma-camera quantification techniques
- 2 groups (Re-186/Sm-153) of whole-body scintigraphic images sets are obtained:
- ✓ 2 sets up to 24h post injection &
- ✓ 2 sets up to 7d post injection

- processing of the obtained images utilizing ROI quantitative methods, previously calibrated with water-phantom measurements, determine residence times and radionuclide uptakes by specific skeletal sites

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Dosimetric calculations

- were performed using site – specific Re–186 and Sm – 153 S values for several source – target combinations within trabecular and cortical bone

along with

- cumulative site – specific activities derived from values obtained by image processing. Skeletal – averaged Re – 186 and Sm – 153 S values were also used.

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Results

- Image processing data revealed higher (2~3 times) lesion uptakes for the group of Sm – 153 patients.
- Time – activity curves for various skeletal sites were generated for both groups of patients.
- Absorbed dose distributions along with time – dose rate curves were derived for both red marrow and different regions of the skeleton.
- Comparisons were made between these parameters and mean absorbed doses calculated using skeletal – averaged S values or/and MIRDOSE3 computer code.

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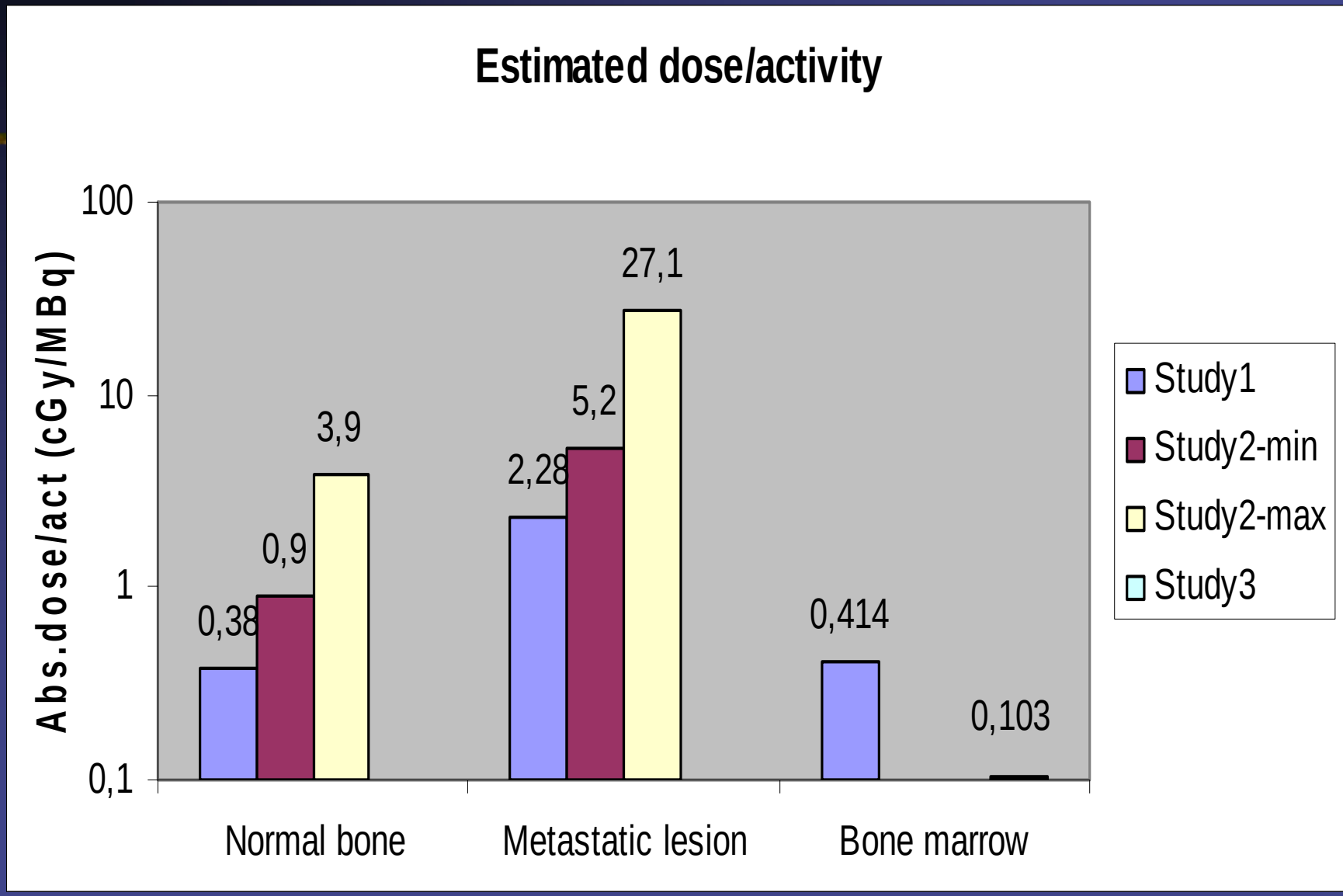

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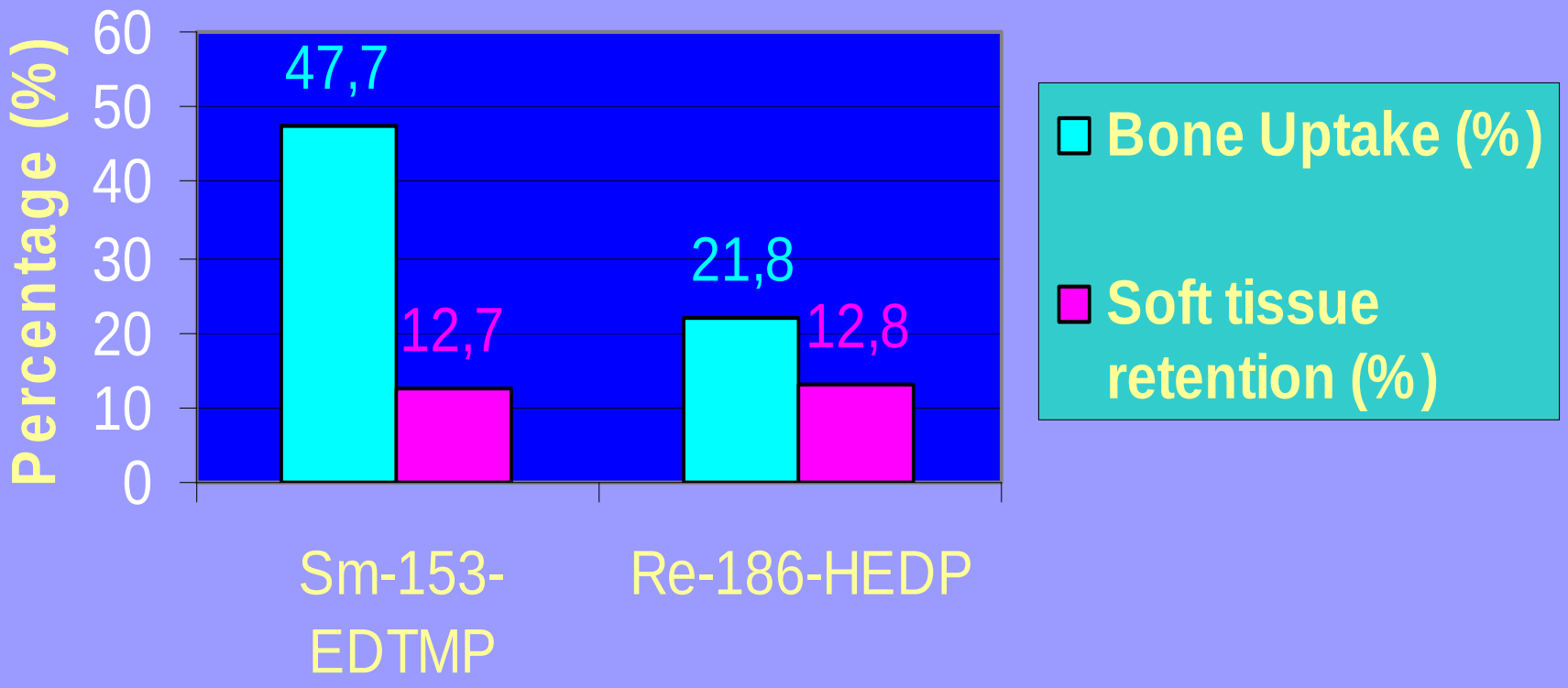
Comparison of Sm-153-EDTMP and Re-186-HEDP



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- Calculations by the MIRD schema, gave absorbed doses per unit volume (voxel) for metastatic and normal bone tissue.
- 2 important parameters were introduced in assessing tumor control probability

M/N: metastatic/normal bone absorbed dose ratio

B/RM: Bone/Red Marrow mean absorbed dose ratio

RADIO-PHARMACEUTICAL	NORMAL BONE abs. Dose mGy/MBq per V U	METATASTATIC LESION abs. Dose mGy/MBq per V U	M / N RATIO *Metastatic /Normal Bone Abs. Dose Ratio*	B/M RATIO *Bone /Marrow Abs. Dose Ratio*
Re 186 HEDP	3.12	16.2	5.2	3.4
Re 188 HEDP	1.80	9.0	5.0	1.9
Sm 153 EDTMP	3.80	22.8	6.0	5.5

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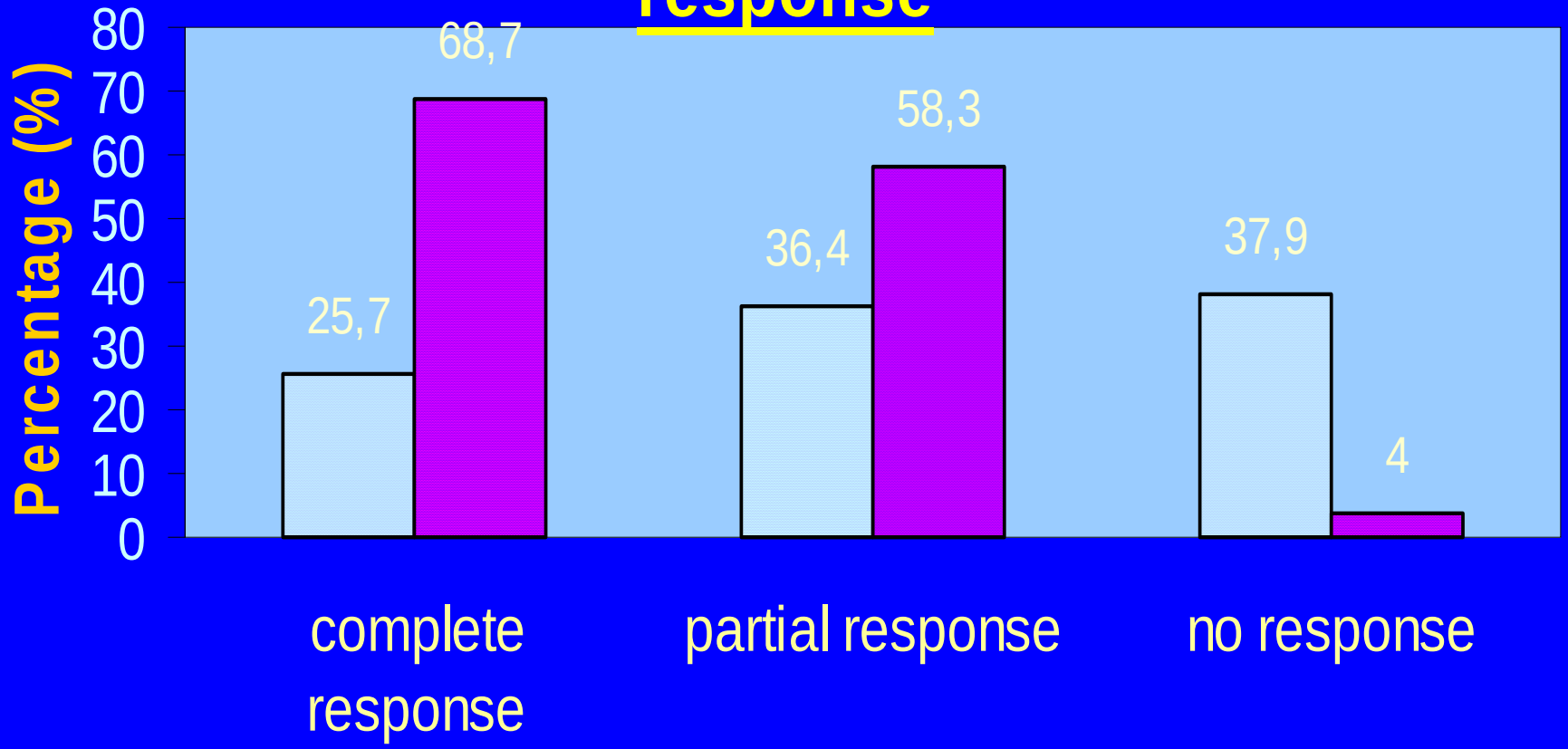
Bone uptake versus therapeutic response



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Conclusions

- Knowledge of dose distribution and time – dose rate curves in Tissues of Interest are crucial parameters for the assessment the relative biological effectiveness of an ongoing treatment.
- They can also predict the possibility of dose – escalation and multiple administrations of the radiopharmaceutical, or
- Therapeutic schemes with external beam irradiation and radionuclide therapy combinations, even combination of different radiopharmaceuticals.

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