The NUKDOS software for treatment planning in MRT

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NUKDOS was developed to provide a software tool for therapy planning in molecular radiotherapy.

Available software packages:

- include only methods for one or several working steps and/or are only commercially available
- do not include an estimate of the overall error of the absorbed doses
Aims

- One software tool for all relevant steps
- Implementation of robust and objective methods
- Calculation of an overall error (uncertainty) for the doses
- User-friendly

→ Improve quality and acceptance of dosimetry
NUKDOS is written in MATLAB

Focus on:
- A series of gamma camera images plus one SPECT/CT (e.g. for PRRT)
- Inclusion of data from
  - External Counting
  - Blood sampling
- MIRD formalism on the voxel level
  - One SPECT/CT (per organ) → voxel based activity
  - Conjugate view gamma camera images → organ/lesion kinetics
  - S values implemented for 3 nuclides → $^{90}$Y, $^{131}$I und $^{177}$Lu
- Includes EANM SOPs for DTC and Benign Thyroid disease
Workflow: Series of planar gamma camera images and one SPECT/CT

2D images processing $R_{2D\text{ organ}} \quad A_{2D\text{ organ}}$ modelling, fit, integration $\int R_{2D\text{ organ}}(t) \cdot dt \quad R_{2D\text{ organ}}(t_{3D})$

Patient scaling:

$A_{i,j,k\text{ organ}}(t_{3D}) \cdot \int R_{2D\text{ organ}}(t) \cdot dt \quad R_{2D\text{ organ}}(t_{3D})$

3D image processing $A_{i,j,k\text{ organ}}(t_{3D}) \quad \bar{a}_{i,j,k\text{ total}}$

calculation of S-values $S_{i,j,k} \quad$ determination of dose coefficients $d_{i,j,k\text{ organ}}$

calculation of the activity to administer $A_{adm}$ dose estimate $D_{\text{ organ}}\text{ BED}_{\text{ organ}}$

target $D,\text{ BED} \quad RC \text{ and } V_{CT} \text{ of organ or tumor}$
Calibration – measurement set-up

SPECT/CT: Symbia T2 (Siemens)
Calibration and quantification
Relative deviations as a function of the effective number of iterations for Lu-177 and I-131
Case:
- Patient with meningioma
- Therapy with $^{90}\text{Y-DOTATATE}$
- Pre-therapeutic dosimetry with $^{111}\text{In-DOTATATE}$

Limit: 12 Gy to kidneys

Activity to administer: 

Dose to spleen, tumour and RM:
NUKDOS-Input

- Basic patient data (name, date of birth, height, weight, sex, notes)
- Administered activity (full/empty syringe, dates, times)
- 3D images (SPECT/CT)
- Gamma camera images
- External counting data
  - Blood/serum samples
  - Urine samples
Starting GUI
CT measured:
Kidney (l.): 194 ml
Spleen: 198 ml
Liver: 1811 ml
Tumour caudal: 87 ml

Total (uncertainty and bias)
Voxel error: 10%

Conditions: quantitative image
2D Image Processing

According to MIRD Pamphlet 16

Validated using UlmDos
Fitting and Model Selection

- Data error (model) specification
- Semi- or fully automated search for starting parameters
- Specification of a priori knowledge of parameter values
- Fit functions (sums of exponentials)
- Model selection using the Akaike Information Criterion (AIC)

Molecular radiotherapy: The NUKFIT software for time-integrated activity coefficient calculation

- Provides a realistic set of functions for NM data
- Minimizes a given objective function
- Provides parameters to determine the quality of the fit
- Provides statistical criteria for choosing the best fit function
- Integrates analytically
- Determines the standard error of the result
- Validated using SAAM2 as comparison

Kletting et al, Med Phys, 2013
Molecular radiotherapy: The NUKFIT software for time-integrated activity coefficient calculation

Choice of fit functions

\[ f_1(t) = A_1 e^{-\lambda_{phys} t} \]
\[ f_2(t) = A_1 e^{-(\lambda_1 + \lambda_{phys}) t} + A_2 e^{-\lambda_{phys} t} \]
\[ f_3(t) = A_1 e^{-(\lambda_1 + \lambda_{phys}) t} + A_2 e^{-(\lambda_1 + \lambda_{phys}) t} \]
\[ f_4(t) = A_1 e^{-(\lambda_2 + \lambda_{phys}) t} + A_2 e^{-(\lambda_1 + \lambda_{phys}) t} \]
\[ f_5(t) = A_1 e^{-(\lambda_2 + \lambda_{phys}) t} + A_2 e^{-(\lambda_1 + \lambda_{phys}) t} + A_3 e^{-\lambda_{phys} t} \]
\[ f_6(t) = A_1 e^{-(\lambda_3 + \lambda_{phys}) t} + A_2 e^{-(\lambda_2 + \lambda_{phys}) t} + A_3 e^{-(\lambda_1 + \lambda_{phys}) t} \]
\[ f_{4A}(t) = A_1 e^{-(\lambda_1 + \lambda_{phys}) t} - A_1 e^{-(\lambda_2 + \lambda_{phys}) t} = A_1 \left[ e^{-\lambda_1 t} - e^{-\lambda_2 t} \right] e^{-\lambda_{phys} t} \]
\[ f_{6A}(t) = A_1 e^{-(\lambda_2 + \lambda_{phys}) t} + A_2 e^{-(\lambda_1 + \lambda_{phys}) t} - (A_1 + A_2) e^{-(\lambda_3 + \lambda_{phys}) t} \]
\[ f_{4B}(t) = A_1 e^{-(\lambda_1 + \lambda_{phys}) t} + (1 - A_1) e^{-(\lambda_1 + \lambda_{phys}) t} \]
\[ f_{6B}(t) = A_1 e^{-(\lambda_1 + \lambda_{phys}) t} + A_2 e^{-(\lambda_2 + \lambda_{phys}) t} + (1 - A_1 - A_2) e^{-(\lambda_3 + \lambda_{phys}) t} \]
Molecular radiotherapy: The NUKFIT software for time-integrated activity coefficient calculation

**Parameters to determine the quality of the fit**

Kletting et al., Med Phys, 2013

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<td>...</td>
<td>Compare with values of other functions</td>
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<tr>
<td>AICc$^c$</td>
<td>$J^d + 2 \leq N^e$</td>
<td>Compare with values of other functions</td>
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<tr>
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<td>All functions $J + 2 \leq N$</td>
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<td>Parameter SE</td>
<td>$J + 1 \leq N$</td>
<td>CV &lt; 25% precise$^g$; CV &lt; 50% acceptable$^h$</td>
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<tr>
<td>Correlation matrix</td>
<td>$J + 1 \leq N$</td>
<td>$-0.8 &lt; $ each element $&lt; 0.8$</td>
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<td>Random distribution</td>
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NukDos

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Fitting
Voxel S Values (VSVs)

- 3 nuclides are supported: $^{90}$Y, $^{177}$Lu and $^{131}$I
- Images with cubical voxels of arbitrary size
- On-the-fly rescaling of pre-tabulated fine-grid Monte-Carlo simulation data obtained with MCNPX

Voxel S Values (VSVs)


Lu-177, VS=3.0 mm

DIE: Dieudonne et al. J. Nucl. Med. 51
REI: Reiner et al. Med Phys 36
MIRD17: Bolch et al. J. Nucl. Med. 40
LAN: Lanconelli et al. Phys Med Biol 57
Therapy Planning

Validated on the organ level with OLINDA/EXM as comparison
Conclusion

NUKDOS can be applied for Dosimetry in PRRT using a series of planar gamma camera images and one SPECT/CT. NUKDOS:

- allows voxel-based dosimetry
- provides an error estimate for the calculated absorbed doses
- allows seamless workflow, no additional software is required
- is freely available (January 2015)

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