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### **ACCEPTED MANUSCRIPT**

#### Development of a calibration protocol for quantitative imaging for molecular radiotherapy dosimetry

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#### Abstract

Within the field of molecular radiotherapy, there is a significant need for standardisation in dosimetry, in both quantitative imaging and dosimetry calculations. Currently, there are a wide range of techniques used by different clinical centres and as a result there is no means to compare patient doses between centres. To help address this need, a 3 year project was funded by the European Metrology Research Programme, and a number of clinical centres were involved in the project. One of the required outcomes of the project was to develop a calibration protocol for three dimensional quantitative imaging of volumes of interest.

Two radionuclides were selected as being of particular interest: iodine-131 ( $^{131}$ I, used to treat thyroid disorders) and lutetium-177 ( $^{177}$ Lu, used to treat neuroendocrine tumours). A small volume of activity within a scatter medium (water), representing a lesion within a patient body, was chosen as the calibration method. To ensure ease of use in clinical centres, an "off-the-shelf" solution was proposed – to avoid the need for in-house manufacturing.

The BIODEX elliptical Jaszczak phantom and 16 ml fillable sphere were selected. The protocol was developed for use on SPECT/CT gamma cameras only, where the CT dataset would be used to correct the imaging data for attenuation of the emitted photons within the phantom. The protocol corrects for scatter of emitted photons using the triple energy window correction technique utilised by most clinical systems. A number of clinical systems were tested in the development of this protocol, covering the major manufacturers of gamma camera generally used in Europe.

Initial imaging was performed with <sup>131</sup>I and <sup>177</sup>Lu at a number of clinical centres, but due to time constraints in the project, some acquisitions were performed with <sup>177</sup>Lu only. The protocol is relatively simplistic, and does not account for the effects of dead-time in high activity patients, the presence of background activity surrounding volumes of interest or the partial volume effect of imaging lesions smaller than 16 ml.

The development of this simple protocol demonstrates that it is possible to produce a standardised quantitative imaging protocol for molecular radiotherapy dosimetry. However, the protocol needs further development to expand it to incorporate other radionuclides, and to account for the effects that have been disregarded in this initial version.

Key Words: molecular radiotherapy, nuclear medicine, quantitative imaging, dosimetry, SPECT, SPECT/CT

#### 1. Introduction

Molecular radiotherapy is a field of medicine in which unsealed radionuclides are administered to patients in order to treat benign or malignant disease. These radionuclides are chelated to molecules designed to target specific tissues or biochemical pathways within the body. By virtue of their preferential uptake within the target tissue and the use of short-range beta- or alpha-emitting radionuclides, these *radiopharmaceuticals* enable high radiation doses to be delivered whilst largely sparing normal tissue. The first recorded use of radium-226 to treat a number of diseases, with the best responses seen in high blood pressure, pernicious anaemia and leukaemia (Proescher, 1913). By the late 20<sup>th</sup> century, there were a handful of molecular radiotherapy treatments in routine clinical use (Hamilton and Soley, 1939; Lawrence, 1940; Pecher, 1942; Siedlin et al., 1948; Werner et al., 1948). More recently, there has been a huge increase in the number of new molecular radiotherapy procedures using radiopharmaceuticals with increasingly specific uptake patterns and exotic radionuclides (Sathekge, 2013). This

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