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Determining and updating PET/CT and SPECT/CT diagnostic reference levels : a systematic review

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1 **Determining and updating PET/CT and SPECT/CT**
2 **diagnostic reference levels: A systematic review**

3 **Short title: DRL for PET/CT and SPECT**

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28 **ABSTRACT**

29 The aim of this systematic review is to investigate the national diagnostic reference level
30 (NDRL) methods for positron emission tomography/computed tomography (PET/CT) and
31 single photon emission tomography/computed tomography (SPECT/CT) procedures. A search
32 strategy was based on the preferred, reporting items for systematic review and meta-analysis
33 (PRISMA). Relevant articles retrieved from Medline, Scopus, Web of Science, Embase,
34 Cinahl, and Google Scholar published up to October 2017. The search yielded 1057 articles.
35 Fourteen articles were included in the review after a screening process. Relevant information
36 from the selected articles were summarised and analysed. Discrepancies were found between
37 the methodologies utilised to establish and report both PET/CT and SPECT/CT NDRLs, e.g.
38 patient sampling and administered activity. Further research should focus on reporting more
39 NDRLs for hybrid PET/CT and SPECT/CT examinations, and establish a robust NDRL
40 standard for the CT portion associated with PET/CT and SPECT/CT examinations. This review
41 provides updated NDRL recommendations to deliver more comparable international radiation
42 doses for administered activity and CT dose across PET/CT and SPECT/CT clinics.

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50 **Introduction**

51 Hybrid modalities integrating positron emission tomography (PET) or single photon emission
52 computed tomography (SPECT) with X-ray computed tomography (CT) enable intrinsic co-
53 registration of functional and anatomical data in a single procedure (PET/CT or SPECT/CT)<sup>(1-
54 3)</sup>. The introduction of hybrid medical imaging technology has revolutionised the practice of
55 diagnostic nuclear medicine (NM). PET/CT and SPECT/CT have wide acceptance for many
56 clinical investigations such as oncology, neurology, cardiology and psychiatry⁽⁴⁾. The CT
57 aspect is often a low-dose CT scan to provide attenuation correction (CT-AC), anatomical
58 localisation (CT-AL), or diagnostic CT procedures with or without contrast media⁽⁴⁻⁶⁾. The
59 fused information from PET or SPECT with CT data can result in superior diagnostic accuracy
60 for localisation, detection, staging and monitoring of many disease mechanisms compared to
61 PET, SPECT or CT alone⁽⁷⁾.

62 A concern with PET/CT and SPECT/CT imaging is the combined radiation doses from both
63 radiopharmaceutical and X-ray CT components^(8, 9). The lifetime attributable risk of cancer
64 incidence for fluoride-18 fluorodeoxyglucose (¹⁸F-FDG) whole-body PET/CT scans for 20-
65 year-old males and females in the United States of America (USA) has been reported to be up
66 to 0.323% and 0.514% respectively⁽¹⁰⁾. Therefore, it is imperative to implement a radiation
67 dose optimisation process by utilising the “as low as reasonably achievable” (ALARA)
68 principle to protect patients from unwarranted high radiation burdens and to minimise the
69 probability of inducing cancer. However, McCullough⁽¹¹⁾ reported there is no reliable evidence
70 to demonstrate risks of medical imaging at low doses (<50 mSv), which includes the majority
71 of NM examinations.

72 The International Commission on Radiological Protection (ICRP) publication 60 introduced
73 diagnostic reference levels (DRLs) in 1990, and its implementation was recommended in the

74 ICRP 73 1996 publication⁽¹²⁾. In 1997, the European medical exposure directive defined DRLs
75 as “dose levels in medical radio-diagnostic practice or, in the case of radiopharmaceuticals,
76 levels of activity, for typical examinations for groups of standard-sized patients or standard
77 phantoms, for broadly defined types of equipment. These levels are not expected to be
78 exceeded for standard procedures when good and normal practice regarding diagnostic and
79 technical performance is applied”⁽¹³⁾. DRLs are advisory in nature and not dose limits. Their
80 role is to draw attention to the issue of radiation protection and safety and thereby reduce the
81 radiation doses to patients. However, one needs to acknowledge that the radiation dose can
82 acceptably exceed the national DRL (NDRL) value in some circumstances due to the patient's
83 characteristics or disease factors that require deviation from standard procedures. The DRLs
84 should be refined over time based on improvements in standard procedures and equipment⁽¹⁴⁾.

85 Implementing DRLs enables identification of variations between high and low dose imaging
86 protocols and equipment⁽¹⁴⁾. This is possible through comparing mean or median local DRL
87 against national or regional DRL for equivalent representative groups of patients undergoing a
88 specific typical procedure. Where the value of the mean or median local DRL dose exceeds the
89 accepted NDRL value without convincing medical justification, this triggers the need for
90 equipment performance or imaging protocol review for dose optimisation⁽³⁾.

91 The DRLs in PET/CT and SPECT/CT are determined by collecting radiation doses from the
92 administered activity (A) measured in megabecquerel (MBq) as well the CT dose in volume
93 CT dose index (CTDI_{vol}) measured in milligray (mGy) and the dose length product (DLP)
94 measured in milligray times centimetre (mGy.cm)⁽¹⁵⁾. Two different measures are used to
95 report DRL values for the A, namely the 75th percentile and guidance level. The 75th percentile
96 method is based on the evaluation of the distribution of median A from participant centres in a
97 national or regional DRL survey. It is used to report the DRLs for both A and CT dose^(16, 17).
98 Evidence gathered by expert professional organisations is used to establish guidance levels on

99 a national level for a standard-sized patient⁽¹⁶⁾. Guidance levels are used to report recommended
100 A but not CT dose.

101 The achievable dose provides an additional reference level for optimising diagnostic imaging
102 without compromising image quality^(18, 19). The achievable dose corresponds to the 50th
103 percentile of the NDRL and is used to identify the dose commonly used in clinical practice.
104 Centres with a local DRL just below the 75th should focus on optimising the acquisition
105 protocol and equipment with an aim to approach the achievable dose^(18, 19).

106 The administered activity duration product (ADP) has been proposed as an additional unit for
107 NM DRLs⁽¹⁹⁾. The ADP is a product of the A and acquisition time (MBq.min). The ADP is
108 considered a better measure for dose optimisation, compared to A (MBq) alone, as A and
109 imaging time both impact on image quality⁽¹⁹⁾. The photon density in a NM image is directly
110 proportional to the ADP. Therefore, administering the same recommended activity to patients
111 in different centres may not yield the same image quality as some facilities will use different
112 total acquisition times due to variations in imaging equipment sensitivity⁽¹⁹⁾. Thus, reporting
113 both MBq and MBq.min units for DRL and ADP reference levels provides additional
114 information about photon flux which impacts on image quality.

115 The establishment of DRLs for PET/CT and SPECT/CT imaging is an essential step in
116 recognising variations between radiation doses delivered to the patient using a diverse range of
117 equipment and changing protocols⁽¹⁴⁾. The existing PET/CT and SPECT/CT, PET, SPECT, and
118 CT component methods are prone to some limitations due to diverse methods implemented for
119 population selection, different reporting methods, the impact of new imaging technology, and
120 reporting effective dose (E) from both the A and CT^(15, 18-30). The purpose of this systematic
121 review is to determine the variations in reported NDRL methodology and values for adult
122 PET/CT and SPECT/CT procedures.

123 **Material and Methods**

124 **Search strategy**

125 A research protocol for the review was selected and designed before undertaking our database-
126 driven research. This included writing a clear protocol to address the research question,
127 followed by creating keywords that would help us search data across a diversity of databases.
128 No industry funding was obtained for this systematic review, which was conducted in line with
129 the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)
130 guidelines. The preferred reporting items for PRISMA methodology was used to search for
131 articles published up to October 2017⁽³¹⁾. A systematic literature search of Medline, Scopus,
132 Web of Science, Embase, and Cinahl was performed to identify the essential articles that
133 established hybrid DRL NM procedures for adult patients. To access more information,
134 reference lists of published articles were examined to identify additional articles not identified
135 in the database searches. Literature Boolean search was performed using the following method
136 and terms: Intervention (“Diagnostic reference levels” or “Diagnostic reference activities” or
137 “DRLs”) AND cohort (“Positron emission tomography/computed tomography” or “Single
138 photon emission computed tomography/ computed tomography” or “Positron emission
139 tomography” or “Single photon emission tomography” or “Computed tomography” or
140 “Nuclear medicine” or “PET/CT” or “SPECT/CT” or “PET” or “SPECT” or “CT” or “NM”)
141 OR other (“PET radiopharmaceutical” or “Radiopharmaceutical”). The search was limited to
142 include all the articles that had been published in the English language.

143 **Criteria for selection**

144 All cohort studies were selected based on the inclusion and exclusion criteria developed,
145 through the use of a population, intervention, comparison, and outcomes (PICO) methodology
146 Table 1. Articles were considered for the review if they described NDRLs of adult patients

147 undergoing PET/CT and SPECT/CT procedures. Articles that did not fulfil these criteria were
148 excluded as were case studies, posters, narrative literature reviews, and case reports. All articles
149 included contained the theme of measurement methods for adult NDRLs with PET/CT and
150 SPECT/CT examinations (Table 1). The funding sources for each selected study were assessed
151 as part of the review.

152 **Quality assessment**

153 The quality assessment was performed by two reviewers (EA and PK). These reviewers
154 developed an Excel data extraction sheet based on the quality assessment tool for quantitative
155 studies, as developed by the Effective Public Health Practice Project (EPHPP)⁽³²⁾. An Excel
156 datasheet was used to assess a study's design, to determine whether it satisfied the data
157 selection criteria. The developed Excel data extraction sheet was used independently by each
158 reviewer to evaluate the risk of bias and to pinpoint any poor-quality or irrelevant publications.

159 **Data extraction** Two reviewers (EK and PK) independently evaluated articles for quality and
160 for risk of bias, to ensure that they satisfied the inclusion criteria. Data extraction was
161 undertaken, based on the following characteristics in each study: hybrid type, equipment,
162 population, reporting for PET or SPECT, reporting method for CTDI_{vol}, reporting method for
163 DLP, and E. The reviewers were aware of large variations among the included studies, in terms
164 of their NDRL methods. Each article was reviewed based on the PICO approach; the extracted
165 data were compared between two reviewers, and wherever there was disagreement, all
166 variations in opinion were subsequently resolved through discussion. An identified article was
167 independently scored as high (1), moderate (2), or low (3) by each reviewer. As recommended
168 by the reviewer, only articles rated as high (1) or moderate (2) by reviewer were included in
169 this review.

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171 **Results**

172 The combined search strategy identified 1057 articles: 169 from MEDLINE (OVID), 278 from
173 Web of Science, 326 from Embase, 265 from Scopus, 17 from CINAHL, and two from Google
174 Scholar. Of these, 413 articles were duplicates and deleted, leaving a total number of 644
175 articles. The 644 articles were assessed for the eligibility, of these, 611 were excluded on initial
176 screening of titles and abstracts. Thirty-three articles met the criteria for a full-text review and
177 were evaluated utilising the inclusion and exclusion criteria of PICO methodology. Nineteen
178 articles were excluded due to insufficient data for evaluation of methods, reporting local DRL,
179 conference, oral presentation, and case report. As a result, fourteen articles met the selection
180 criteria as shown in Figure 1. All studies were rated high and moderate and were used to
181 assess variations in the determined NDRL method and values among adult patients undergoing
182 PET/CT and SPECT/CT procedures. Two NDRL articles reported funding support for their
183 surveys, but the other did not. These two articles were funded by the Japanese Society of
184 Nuclear Medicine⁽²¹⁾, while the other article was funded by The English Department of
185 Health⁽²⁹⁾.

186 A summary of the fourteen articles is illustrated in Tables 2 and 3. Two countries have
187 established the NDRL for PET/CT and one for SPECT/CT examinations. Most NDRL
188 publications were related to either PET or SPECT component and two for CT component only.
189 Seven NDRL articles were from Europe^(18, 20, 24, 25, 27, 29, 30), two from the United States of
190 America^(19, 23), two from Brazil^(22, 26), and single articles from Australia and New Zealand⁽²⁸⁾,
191 Korea⁽¹⁵⁾ and Japan⁽²¹⁾. The articles were published between 2002 to 2017, with the majority
192 published between 2013 to 2017.

193 The methodology for determining patient selection varied. Two common methods for selecting
194 the patient sample reported in the literature were weight and non-weight restriction. The weight

195 restriction method involves selecting at least 20 patients whose weights are 70 ± 10 or 75 ± 25
196 kg^(25, 27, 28). Three articles reported NDRL values based on weight criteria for PET/CT and PET
197 examinations. The non-weight restriction method involved selecting a range of 1 to 76 patients
198 for each PET/CT, SPECT/CT, PET, SPECT, and CT component associated with PET and
199 SPECT examinations. Six articles adopted non-weight restriction approach^(15, 18-20, 23, 24) and
200 five articles did not provide any details of the patient sampling^(21, 22, 26, 29, 30).

201 The most frequent imaging procedures were ^{18}F -FDG PET and $^{99\text{m}}\text{Tc}$ - methyl diphosphonate
202 (MDP) SPECT bone scans with a range of reported NDRLs for an A of 200 to 592 MBq and
203 600 to 999 MBq, respectively (Table 2 and 3). Some of the identified articles reported clinical
204 indications for PET/CT and SPECT/CT examinations. A total of six articles identified tumours
205 for PET/CT examinations. Of the six articles, two reported the ^{18}F -FDG value used for both
206 tumour and infection/inflammation clinical indication. Only one article reported the common
207 clinical indications for six SPECT/CT examinations and the other article reported the clinical
208 indication for SPECT/CT thyroid metastasis^(18, 24).

209 There were five manufacturers of PET/CT and SPECT/CT equipment using six different NM
210 detectors installed between 2000 and 2015 reported (Table 4). Two articles reported both the
211 manufacturer and model of PET/CT equipment^(15, 24). One article reported the number CT rows
212 only, e.g. 2 and 16 slice⁽²⁴⁾. One article reported CT-AC and AL acquisition parameters
213 associated with a ^{18}F -FDG whole-body scan, while another article reported scan length for six
214 PET/CT and SPECT/CT examinations^(18, 23).

215 A NDRL for the CT component used for AC and AL and AC only was reported in three and
216 one article, respectively^(15, 18, 23, 24, 27). No authors reported the NDRL for the CT component
217 when used for diagnostic CT. All ^{18}F -FDG PET/CT whole body CTDI_{vol} values were lower
218 than the NDRL of 15 mGy, as reported by the Australian Radiation Protection and Nuclear
219 Safety Agency (ARPANSA) for diagnostic chest CT⁽³³⁾.

220 Different approaches were used to report NDRL in the review. Twelves articles reported NDRL
221 values based on the 75th percentile^(15, 18-23, 26-30), and two articles based on guidance level^(24, 25).
222 In addition to the NDRL, two articles also reported achievable dose and one article reported
223 ADP^(18, 19). There were seven articles reported their recommended A strategy, e.g. MBq/kg^{(15,}
224 ^{19-21, 25-27)}. Two articles reported NDRLs for ¹⁸F-FDG based on TOF technology^(20, 27).
225 Seven articles reported the E, three articles for both A and CT^(15, 24, 27), three articles for A
226 only^(22, 29, 30) and one article for the CT only as seen in Tables 2 and 3.

227 **Discussion**

228 The patient selection methods used to determine the NDRL for PET/CT, SPECT/CT, PET,
229 SPECT and CT for hybrid imaging procedures were varied, see Table 2 and 3. The weight
230 restriction and non-weight restriction are two commonly accepted methods for selecting
231 patient's sample for DRL survey. The weight restriction method involves selecting at least 20
232 to 30 standard size patients, with the mean weight of patients in the sample being 70 ± 5 kg⁽³⁾.
233 For the current European NDRL project, another patient weight criteria was 70 ± 15 kg; the
234 number of samples collected using the survey was not mentioned⁽³⁴⁾. Several NDRL articles
235 have indicated the patient weight and these are presented under the patient characteristics of
236 patient samples in Tables 2 and 3. Watanabe et al. argue that it is necessary to conduct NDRL
237 articles based on weight restriction criteria because of variations in patient habitus and weight
238 may have an impact on the results⁽²¹⁾. The weight restriction method allows data comparison
239 with other published NDRL using the same approach for PET/CT and SPECT/CT imaging.
240 For the non-weight restriction method, some NDRL methods for NM, PET/CT and SPECT/CT
241 examinations were used to collect all present patients during a time frame acceptable for the
242 NDRL survey⁽³⁾. The non-weight restriction method has some advantages compared to weight
243 restriction method. Applying the weight limit criteria for the population sample may reduce the
244 availability of data and extend the data collection period^(16, 35). Using the NDRL method

245 without weight restriction may result in a larger patient sample, which should lead to improved
246 understanding of patient weights in a national population ⁽³⁵⁾.

247 The literature showed the numbers of patients sampled using weight and non-weight restriction
248 methods ranged from 1–76 patients. For the weight restriction method, the patient samples
249 ranged from 20–30 patients with different weight-standard criteria^(20, 25, 27). However, two
250 articles reported NDRLs based on sample sizes that were too small (for example, lower than
251 ten patients)^(19, 24). For the non-weight restriction method, the samples varied and were
252 collected over different time frames, which ranged from four months to one year. Iball et al.
253 demonstrated UK's NDRL method aimed to collect 30 patients over five months for PET/CT
254 and SPECT/CT examinations⁽¹⁸⁾. Iball et al. concluded that patient weight data only existed for
255 a small number of PET/CT and SPECT/CT examinations; therefore, the UK's NDRL method
256 was limited to reports of NDRLs based on a standard patient size of 70 ± 10 kg⁽¹⁸⁾. The average
257 number of patients in the non-weight restricted NDRL articles was 38. The current ICRP 135
258 recommends when collecting 50 or more patients during NDRL survey, weight restriction is
259 not required⁽³⁾. However, some authors found similar NDRL results, less than 2% difference,
260 when using either weight or non-weight restriction method^(36, 37). Future PET/CT and
261 SPECT/CT NDRL methods should involve a minimum of 50 patients with a non-weight-
262 restriction approach⁽³⁾. A NDRL method based on the selection of a large number of patient
263 sample enables filtering the data by different patient body sizes better enabling NDRL data
264 comparison^(38, 39), e.g. retrospectively selecting 30 patients with weight restriction (70 ± 15 kg)
265 acquired from a non-weight-restriction data^(18, 20, 40).

266 Some articles reported PET/CT, PET and SPECT/CT NDRLs for clinical indications. Iball et
267 al. provide ¹⁸F-FDG PET/CT NDRL, CTDI_{vol} and DLP, for two clinical indications for half
268 body imaging and ^{99m}Tc-phosphates SPECT/CT NDRL, CTDI_{vol} and DLP, for six common
269 clinical indications for bone imaging⁽¹⁸⁾. Willegaignon et al. demonstrated that the amount of

270 ¹⁸F-FDG A for the most PET/CT common indications related to oncological and
271 infection/inflammation was 350 MBq⁽²²⁾. The European Association of Nuclear Medicine
272 (EANM) guidelines illustrate that administered activity of ^{99m}Tc-MDP is 370-740 MBq for the
273 most common clinical indications for three phase or whole body SPECT/CT bone scans⁽⁴¹⁾.
274 The literature reveals that the recommended NDRL for A will be the same for common patient
275 clinical indications in relation to PET/CT and SPECT/CT procedures. The amount of A differs
276 when different radiopharmaceuticals are used for different PET/CT and SPECT/CT procedures
277 (Table 2 and 3).

278 Body region was another area that varied across studies. Several publications have asserted that
279 variations in CT scan range or body region associated with oncological PET/CT protocols and
280 SPECT/CT bone protocols depend on patient clinical indication demonstrating a lack of
281 standardisation⁽⁴²⁻⁴⁵⁾. For ¹⁸F-FDG PET/CT procedures the most common CT range was varied
282 from the mid-femora to the external auditory meatus, and from the top of the head to the feet
283 for tumours that show a high probability of metastasis in the brain, skull or lower extremities,
284 e.g. melanoma. A more limited CT range for tumour imaging may be considered when a patient
285 returns for follow-up imaging^(6, 46). The literature reveals that the reported NDRL DLP values
286 for ¹⁸F-FDG whole body PET/CT scans varied from 400 to 750 mGy.cm due to various scan
287 range descriptions, with only one NDRL article providing the scan range for the most common
288 clinical indications related to ¹⁸F-FDG whole body scans^(15, 18, 27). ARPANSA reported that the
289 NDRL for PET/CT and SPECT/CT examinations takes into account the scan region and the
290 CT used for the AC or AL to cover a wide range of clinical indication for each examination⁽³³⁾.
291 The first and second scan ranges for the whole body CT protocol are started from the eyes to
292 the thighs and from the vertex to the toes, respectively. For SPECT/CT, Gardner et al. provides
293 local DRL values for bone and neuro-endocrine SPECT/CT procedures takes into account
294 different anatomical body regions and the purpose of CT used for each anatomical regions⁽⁴⁵⁾.

295 Four different anatomical body regions were identified for neuro-endocrine SPECT/CT
296 procedures known as abdomen, abdomen/pelvis, chest/abdomen/ pelvis, and
297 head/chest/abdomen/pelvis and the DLP values for each anatomical body region were 280,
298 204, 204, and 377, and 373 mGy.cm respectively⁽⁴⁵⁾. Furthermore, the scan length might be
299 increased if the NM physician found a new metastatic lesion requiring additional CT
300 investigation⁽¹⁸⁾. However, scan length is a crucial parameter influencing a patient's CT dose
301 and is directly associated with DLP⁽¹⁸⁾. A longer scan length involves a greater number of slices
302 over a larger anatomical region, which subjects the patient to higher radiation exposure. Iball
303 et al. suggested that limiting the scan length to only the area requiring investigation would
304 optimise radiation doses delivered from PET/CT and SPECT/CT examination used in British
305 clinical centres⁽¹⁸⁾. Thus, an NDRL method for PET/CT and SPECT/CT should provide a clear
306 description of the clinical indications in relation to PET/CT and SPECT/CT examinations, the
307 administered radiopharmaceutical, and the scan range of anatomical regions^(18, 33, 45).

308 Improvements to PET/CT and SPECT/CT hardware and software allow a reduction in radiation
309 exposure to patients or shorter scanning times while maintaining acceptable image quality⁽⁴⁷⁾.

310 Recent improvements to PET and SPECT include additional scanner rings for PET,
311 scintillation detector materials including cadmium-zinc-telluride (CZT) detectors with novel
312 collimators for SPECT, and reconstruction algorithms which incorporate time of flight (TOF)
313 and point spread function (PSF) modelling^(40, 48). Kwon et al. demonstrate that using a PET/CT
314 unit equipped with TOF technology and PSF algorithms required less administered activity⁽¹⁵⁾.

315 Two articles reported NDRL for ¹⁸F-FDG whole-body based on TOF technology. Roch et al.
316 and Etard et al. reported that the A for ¹⁸F-FDG whole-body scans decreased from 360 to 260
317 MBq and from 300 to 250 MBq with PET/CT systems equipped with TOF technology,
318 respectively^(20, 27). However, Roch et al. noted that insufficient numbers of centres with
319 SPECT/CT units equipped with CZT participated in the survey, therefore, appropriate NDRL

320 could not be provided for this new technology⁽²⁰⁾. Furthermore, innovations in CT components,
321 including automatic tube current modulation, automatic tube voltage selection (ATVS), and
322 iterative image reconstruction algorithms, enable minimisation of radiation dose without
323 compromising image quality⁽⁴⁹⁾. Kwon et al illustrate that CT AC and AL radiation doses
324 delivered from CTDI_{vol} and DLP were significantly reduced with the use of a recently installed
325 PET/CT instrument⁽¹⁵⁾. Many authors assert that current technical innovations in PET/CT and
326 SPECT/CT modality enable a reduction in radiation exposure to the patients and while
327 maintaining image quality^(47, 49). However, the literature reveals that no image quality criteria
328 exist to assess PET and SPECT image quality; nor are there any criteria for CT to assess AC
329 and/or AL image quality associated to PET and SPECT examinations. In diagnostic radiology,
330 an expert group of radiologists and physicists published European guidelines on quality criteria
331 for CT⁽⁵⁰⁾. The main objective of the European guidelines is to provide minimum CT radiation
332 dose while ensuring the obtainment of acceptable image quality criteria. Thus, NM researcher
333 should develop methods to explore the acceptable balance between scan time and should
334 develop image quality criteria and patient radiation dose reductions for PET/CT and
335 SPECT/CT imaging modalities. It is recommended that when reporting NDRL the study takes
336 into the account the manufacture date of equipment, and the current technological advances in
337 PET/CT and SPECT/CT equipment, e.g. TOF and CZT scintillation detectors, respectively, as
338 these technologies enable a reduction in the administered dose.

339 Some authors recommended that the achievable dose and ADP be used as supplementary dose
340 measures for PET/CT and SPECT/CT NDRLs for identifying radiation doses yield suitable
341 diagnostic image quality^(18, 19). Iball et al. found that CT doses vary significantly for the same
342 procedures and the same clinical indication and conclude that radiation doses may be reduced
343 by establishing both DRLs and achievable dose for British clinical practices⁽¹⁸⁾. Alessio et al.
344 argues that NDRL and achievable dose reference levels for PET and SPECT A are limited as

345 they do not consider the impact of total acquired photons on image quality⁽¹⁹⁾. Alessio et al.
346 recommends including ADP, which incorporates acquisition time, with NDRL as a practical
347 way to overcome this limitation⁽¹⁹⁾. Determining ADP is a challenge for PET or SPECT
348 examinations, due to variations in A and scan duration among clinical centres. Some clinical
349 centres reduce A to patients and increase scan duration to maintain image quality. However, a
350 drawback of increased scan duration is that some patients are unable to remain still for long
351 durations, resulting in motion artefacts which degrade image quality⁽³⁾. In some circumstances,
352 scanning obese patients required an increase in the A to ensure the maintenance of diagnostic
353 image quality. From a radiation protection point of view, increasing A to patients minimises
354 scan duration and should not be performed on the basis of increased department workflow⁽³⁾.
355 However, only one article reports on ADP quantity, so the usefulness of the collection of the
356 scan duration to assist in the determination of the ADP has not been fully explored. From the
357 authors' perspective, it is important to determine the ADP to identify the normal clinical
358 practice and understand the trade-off between the A and the scan duration required to maintain
359 diagnostic image quality. Alessio et al. reported the ADP values for ¹⁸F-FDG PET/CT and
360 ^{99m}Tc-MDP SPECT/CT scans to provide clear guidelines for clinical practice to ensure the
361 obtainment of sufficient image quality⁽¹⁹⁾. The authors illustrate that determining the ADP
362 requires the collection of the administered activity and scan duration during the NDRL survey
363 from participant clinical centre, which is easy to perform. The authors conclude that if the ADP
364 value is consistently higher than the reported national ADP values, then the clinical practice
365 should optimise the A, adjust the scanning time or both to ensure that sufficient image quality
366 is obtained⁽¹⁹⁾. Therefore, future PET/CT and SPECT/CT NDRL methods should report both
367 75th percentile (DRL) and 50th percentile achievable dose to encourage clinical centres to
368 optimise and improve their clinical practice. NDRL methods should collect data on A and
369 acquisition time to evaluate the value of ADP, as a DRL metric.

370 All but one of the presented PET/CT and SPECT/CT NDRL methods failed to report the details
371 of CT acquisition protocols⁽²³⁾. Investigating radiation doses delivered from different CT
372 acquisition protocols aids in dose optimisation⁽⁸⁾. However, the details of the acquisition are
373 important to investigate the differences between NDRLs and to assist with optimisation. The
374 NDRL method should be easy to perform and serve as a guideline to ensure that the median
375 radiation dose metric delivered from clinical centres is equal to or lower than the recommended
376 75th percentile of the NDRL standard^(3, 19). The reported NDRL values should be used as a way
377 to underpin optimisation strategies. The optimisation process is separate to the DRL process
378 and should be initiated at the level of clinical practice when the median radiation dose quantity
379 of clinical centre exceeds the 75th percentile of NDRL standard without justifiable reason^(3, 19).
380 Optimising CT components associated with PET/CT and SPECT/CT procedures would be
381 achieved by modifying CT acquisition parameters, such as by lowering kVp and mAs values,
382 or selecting a larger pitch ratio without compromising diagnostic image quality⁽⁸⁾. It is practical
383 to report the NDRL standard and collect the CT parameters to understand the details of CT
384 acquisition protocol and variation between all participant centres. Jallow et al. reported the
385 NDRL for CTDI_{vol} and collected all CT acquisition parameters associated with ¹⁸F-FDG
386 oncological imaging procedures in United States PET/CT clinical centres⁽²³⁾. They
387 demonstrated that the 75th percentile of CTDI_{vol} associated with ¹⁸F-FDG PET/CT oncological
388 procedures was 9.8 mGy. Their results highlighted a wide range of CT acquisition parameters
389 among participants clinical centres such as tube current, pitch ratio and collimation, which
390 ranged from 20–450 mA, 0.5–2, and from 5–40 mm, respectively⁽²³⁾. The diversity of CT
391 acquisition parameters indicates there is an opportunity to optimise CT acquisition protocols
392 for ¹⁸F-FDG whole-body PET/CT examinations. Thus, it is more practical to report PET/CT
393 and SPECT/CT NDRL methods and report the details of the CT acquisition protocol to assist
394 in the development of dose optimisation strategies⁽²³⁾.

395 NDRL units for A are either A (MBq) or A per unit of body weight (MBq/kg). The
396 recommended A depends on several factors such as equipment type, patient weight, acquisition
397 protocol and reconstruction method^(6, 51). It is important to illustrate that weight-based A is not
398 appropriate for some SPECT/CT examinations, in which the A is concentrated in a single
399 organ, such as thyroid and sentinel node examinations, as well as pulmonary ventilation and
400 perfusion examination⁽³⁾. The methods that NM clinics use to determine A to patients are
401 varied, some use fixed methods or follow international guidelines, while others use weight-
402 based methods⁽²⁶⁾. Alessio et al. examined different strategies for A for ¹⁸F-FDG whole-body
403 PET/CT and ^{99m}Tc-MDP SPECT bone examinations⁽¹⁹⁾. They reported no statistical
404 differences in the average A for fixed, range, and weight-based strategies. They also found that
405 PET/CT (n=3) and SPECT/CT (n=1) mobile clinics delivered higher radiation doses than the
406 non-mobile clinics by 30% and 40%, respectively, due to the utilisation of fixed methods for
407 determining A⁽¹⁹⁾. Oliveria et al. illustrate that adjusted ¹⁸F-FDG weight-based strategies
408 greatly varied among two clinics using PET/CT equipment from the same manufacturer and
409 with same scintillation detectors (3.7 MBq.kg⁻¹ to 7.4 MBq.kg⁻¹), illustrating a lack of
410 standardisation and a potential to optimise the ¹⁸F-FDG dose⁽²⁶⁾. Roch et al. claimed that the A
411 recommendations should be determined based on patient weight⁽²⁵⁾. Adopting weight-based
412 strategy enables to explore the variations for the A between clinical centres. Thus, NDRL
413 surveys should report the recommended administered strategy based on patient weight
414 (MBq/kg) for all PET/CT and SPECT/CT examinations in order to provide suitable guidelines
415 for clinical centres⁽²⁵⁾.

416 The effective dose (E) was also reported for the majority of PET/CT, SPECT/CT, PET, SPECT
417 and CT components associated with PET and SPECT procedures during NDRL surveys
418 (Tables 2 and 3)^(15, 18, 22, 24, 27, 29, 30). The E from PET/CT and SPECT/CT is defined as the sum
419 total of the radiation dose (mSv) from the A and from the CT components allowing

420 quantification of total radiation exposure ($\text{Total E (mSv)} = E_{\text{NM}} + E_{\text{CT}}$) and radiation risk^(52, 53).
421 The E method in PET/CT and SPECT/CT is calculated by multiplying each radiation dose by
422 specific conversion coefficients assigned for the A and the DLP value for the CT dose⁽⁵²⁾. Some
423 researchers used the Monte Carlo software programme to calculate the E value for CT doses
424 such as CT-Expo software version 2.1 and 2.4 (Medizinische Hochschule Hannover Germany)
425 and ImpACT scan CTDI dosimetry software (version 1.0.4 with the National Radiological
426 Protection Board (NRPB) SR250 dose data)^(15, 23, 24, 27). However, E methods are based on
427 assumptions about patients that are not commonly true due to variation in size and physiology.
428 At the moment, the E methods described seem straightforward; however, the results of E values
429 are prone to a lack of precision. Calculating E for the A requires multiplication by a conversion
430 coefficient taken from the ICRP tables. The result of E from CT varies amongst different CT
431 dosimetry software due to the various methods and algorithms utilised for each software
432 program⁽⁵⁴⁾.
433 Reporting E is the only way to merge the radiation doses into one metric from the total radiation
434 doses delivered from PET/CT and SPECT/CT examinations. The reporting of E from PET/CT
435 and SPECT/CT procedures enables us to understand the variation of radiation doses delivered
436 from each radiation dose component and supports a dose optimisation strategy. However, the
437 ICRP 135 publication illustrates that reporting the E should not be a part of NDRL methods⁽³⁾.
438 It is impractical to use E comparisons when a wide range of patients' ages and genders are
439 being compared because it is subjected to large uncertainty⁽⁴⁰⁾. Shrimpton et al explained that
440 E data were excluded from the UK NDRL survey because E has a different purpose than
441 NDRL⁽⁵⁵⁾. The exact method for calculating E is complex and requires collecting extra
442 information about patients' individual biokinetics, physiological and anatomical properties for
443 A and a number of CT parameters such as beam energy and beam filtration⁽³⁶⁾. The E is subject
444 to much uncertainty; therefore, it is not yet recommended to be a part of NDRL methods⁽³⁾.

445 Further research is required to investigate the role of E in developing dose optimisation
446 strategies.

447 **Recommendations**

448 Based on this extensive review, we suggest the following recommendations:

- 449 1. It is recommended that PET/CT and SPECT/CT NDRL methods adopt a non-weight
450 restriction approach and then filter the data acquired for the purpose of international
451 data comparison.
- 452 2. A clear description of the administered radiopharmaceutical and scan range for CT
453 components should be provided for each PET/CT and SPECT/CT examination.
- 454 3. NDRL methods should assess the usefulness of achievable dose and ADP as a DRL
455 metric for A.
- 456 4. It is recommended that NDRLs report the DRLs for PET/CT and SPECT/CT
457 procedures for equipment equipped with or without TOF and CZT technology.
- 458 5. Reporting the NDRL with details of CT acquisition parameters will underpin the dose
459 optimisation strategy programme.
- 460 6. It is recommended that NDRLs of PET/CT and SPECT/CT report the A per patient
461 weight for each exam.
- 462 7. Finally, the E value should not be reported as NDRL metric as it is based on a number
463 of assumptions impacting on its accuracy.

464 **Conclusion**

465 The literature shows differences in methods for establishing DRLs for PET/CT and SPECT/CT
466 examinations. Findings also show variations in reported PET/CT and SPECT/CT DRLs arise
467 from patient characteristics, methods reporting, and progress of the technology. NM
468 professions should report both radiation doses from the A and the CT dose used for different

469 purposes rather than report a separate NDRL for A or CT dose. Further research should be
470 performed to assist in the international standardisation of data collection and reporting of
471 NDRL PET/CT, with more attention given to SPECT/CT procedures.

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652 [/file/349188/PHE_CRCE_013.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/349188/PHE_CRCE_013.pdf).

661 Table 1. Criteria for determining study eligibility.

Characteristics	Criteria
Study year	Articles published up to October 2017.
Study type	Cohort studies
Population	Adult patients undergoing PET/CT and SPECT/CT examination
Intervention	Adult DRL measurement methods for PET/CT and SPECT/CT examinations
Comparator	Reliability of DRL methods for adult in PET/CT and SPECT/CT examinations Reproducibility of DRL methods for adult in PET/CT and SPECT/CT examinations
Outcomes	PET/CT and SPECT/CT DRL methods for adult patients.

662

663 Table 2. Summary of hybrid PET/CT DRL methods.

Authors (Years & Country)	Procedure	Clinical indication	Radiotracer	Scan range	Characteristic of patient sample	DRL dosimetry value		E (mSv)		
						A(MBq) [MBq/kg]	CTDI _{vol} and DLP (mGy) & (mGy.cm)	A	CT	Total
Kwon et al ¹⁵ (KO, 2016)	Whole body	-	¹⁸ F-FDG	Base of skull- upper thigh	10 per each exam	370 [5.89±1.46]	5.96 and 560	5.89	6.26	12
Etard et al ²⁷ (FR, 2012)	Whole body	-	¹⁸ F-FDG	At least neck- thigh	20 (50-100 kg)	350 [4.3] 250 [3.5 TOF]	8 and 750	5.7	8.6	14
Iball et al ¹⁸ (UK,2017)	Half body	Tumour Infection/ Inflammation	¹⁸ F-FDG	Base of brain- mid thigh	30 per each exam	-	4.3 and 400	7.6	6.5	14
Roch et al ²⁰ (FR, 2017)	Whole body	-	¹⁸ F-FDG	-	30 per each exam	350 260 [3.6 TOF]	- -	- -	- -	- -
Watanabe et al ²¹ (JP, 2016)	Tumour	Tumour	¹⁸ F-FDG HP	-	-	235 [2-5]	-	-	-	-
	Tumour	Tumour	¹⁸ F-FDG (Delivery)	-		252 [2-5]	-	-	-	-
	Tumour	Tumour	¹⁸ F-FDG HP	-		227	-	-	-	-
	Brain	-	¹⁸ F-FDG (Delivery)	-		255	-	-	-	-
		-	¹⁵ O-CO ₂ g: 2D	-		7500	-	-	-	-
		-	¹⁵ O-O ₂ g: 2D	-		4500	-	-	-	-
		-	¹⁵ O-CO g: 2D	-		3000	-	-	-	-
		-	¹⁵ O-CO ₂ g: 3D	-		2888	-	-	-	-

664 Table 2. Summary of hybrid PET/CT DRL methods (continued).

665

Authors (Years & Country)	Procedure	Clinical indication	Radiotracer	Scan range	Characteristic of patient sample	DRL dosimetry value		E (mSv)		
						A (MBq) [MBq/kg]	CTDI _{vol} and DLP (mGy) & (mGy.cm)	A	CT	Total
Watanabe et al ²¹ (JP, 2016)	-	-	¹⁵ O-O ₂ g: 3D	-	-	6600	-	-	-	-
	-	-	¹⁵ O-CO g: 3D	-	-	7125	-	-	-	-
	Myocardial/ Metabolism	-	¹⁸ F-FDG H	-	-	221	-	-	-	-
	Myocardial/ Metabolism	-	¹⁸ F-FDG D	-	-	251	-	-	-	-
	Myocardial/ Perfusion	-	¹³ N-NH ₃	-	-	718	-	-	-	-
Jallow et al ²³ (US,2016)	Oncology	-	¹⁸ F-FDG	-	2010-14: 35, 65, 76, 42 and 14 cases	-	9.8, 9.8, 10.2, 9.7 and 9.7	-	-	-
Willegaignon et al ²² (BR, 2015)	Oncology/ inflammation	Tumour/ Inflammation	¹⁸ F-FDG	-	-	370	6.76±1.08	-	-	-
	Brain	-	¹⁸ F-FDG	-	-	350	5.11±1.52	-	-	-
	Bone	-	¹⁸ F-NaF	-	-	370	7.30±0.30	-	-	-
Alessio et al ¹⁹ (USA, 2015)	Whole body	-	¹⁸ F-FDG	-	1-5 (4.3±1.3) cases	592	-	-	-	-
Oliveria et al ²⁶ (BR, 2013)	¹⁸ F-FDG PET	Cancer	¹⁸ F-FDG	-	-	387.7 [5-5.4]	-	-	-	-
Roch et al ²⁵ (FR, 2013)	¹⁸ F-FDG PET	-	¹⁸ F-FDG	-	20 (60-80 kg)	350 and 337 [5]	-	-	-	-

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667 Table 2. Summary of hybrid PET/CT DRL methods (continued).

Authors (Years & Country)	Procedure]	Clinical indication	Radiotracer	Scan range	Characteristic of patient sample	DRL dosimetry value		E (mSv)		
						A(MBq) [MBq/kg]	CTDI _{vol} and DLP (mGy) & (mGy.cm)	A	CT	Total
Botros et al ²⁸ (AU & NZ, 2009)	Whole body	Tumour	¹⁸ F-FDG	-	20 per exam or facility guidance level for 70-80 kg	385	-	-	-	-
	Brain	-	¹⁸ F-FDG	-		385	-	-	-	-
	Myocardial Viability	-	¹⁸ F-FDG	-		370	-	-	-	-
Hart et al ²⁹ (UK, 2005)	Tumours PET	Tumour	¹⁸ F-FDG	-	-	400	-	7	-	-
Brix et al ³⁰ (DE, 2002)	Oncology	-	¹⁸ F-FDG	-	-	370 (2D)	-	7	-	-
	Neurology	-				200 (3D)	-	3.8	-	-
	Cardiology	-								
	Other application	-								

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Note: TOF= Time of flight, ¹⁵O-CO₂= ¹⁵Oxygen Carbon dioxide, ¹⁵O-CO ₁₅= ¹⁵Oxygen Carbon monoxide, HP= hospital product,, g= gas, ¹³N-NH₃= N13 ammonia, NaF= Sodium Fluoride,, A.A =administered activity.

682 Table 3. Summary of hybrid SPECT/CT DRL methods.

Authors (Years & Country)	Procedure	Clinical Indication	Radiotracer	Characteristic of patient sample	DRL dosimetry value		E (mSv)		
					A (MBq) [MBq/kg]	CTDI _{vol} and DLP (mGy) & (mGy.cm)	A	CT	Total
Iball et al ¹⁸ (UK, 2017)	Bone	Bone*	^{99m} Tc-phosphates	30 per each exam	-	4.9 and 150	3.9	-	-
	Parathyroid	Adenoma	^{99m} Tc-sestamibi		-	5.6 and 170	8.1	1.4	9.5
	Post-thyroid ablation	Post-thyroid Ablation*	¹³¹ I-iodide		-	5.9 and 210	-	1.5	-
	Tumour MIBG	Tumour MIBG*	¹²³ I-MIBG		-	5.5 and 240	5.2	-	-
	Octreotide	Octreotide*	¹¹¹ In-octreotide		-	5.5 and 240	11.9	3.3	15.2
	Myocardial	Myocardial*	^{99m} Tc-sestamibi	-	2.1 and 3.6	7.2* and 6.3	0.9*	8.1	
Avramova-Cholakova et al ²⁴ (BG, 2015)	Breast	-	^{99m} Tc-sestamibi and tetrofosmin	H _{1,2} , and ₃ :64, 9, and 18	700	3 and 100	6.3, 5.9, and 2.8	3.2, 1.7, and 1.5	9.5, 7.6, and 4.3
	Bone	-	^{99m} Tc-MDP	H _{1,3} , and ₄ :42, 35, and 13	600	3 and 200	2.5, 3.4, and 2.9	1.2, 1.8, and 7.2	3.8, 5.1, and 10.1
	Thyroid	-	^{99m} Tc-pertechnetate	H ₁ :14	74	4 and 170	1	3.6	4.6
	Parathyroid	-	^{99m} Tc-sestamibi	H _{1,2} , and ₃ :7, 10, and 10	120	2.6 and 100	7.4, 6, and 5	4.1, 2.3, and 1	11.5, 8.3, and 2
	Thyroid	Metastasis	¹³¹ I-iodide	H _{1,1} and ₂ : 12,7, and 10	185	4 and 170	167, 167, and 74	1, 0.5, and 2.4	-
	Lymphatic	-	^{99m} Tc-Nanocoll	H ₁ and ₂ :10 and 20	74	4 and 120	0.3 and 0.2	2.8 and 2.1	3.1 and 2.2
	Lung perfusion	-	^{99m} Tc-MAA	H _{2,3} , and ₄ : 20, 14, and 19	20	2.6 and 100	1.1, 2, and 2	1.4, 1.3, and 8.5	2.5, 3.3, and 10.5

684 Table 3. Summary of hybrid SPECT/CT DRL methods (continued).

Authors (Years & Country)	Procedure	Clinical indication	Radiotracer	Characteristic of patient sample	DRL dosimetry value		E (mSv)		
					A (MBq) [MBq/kg]	CTDI _{vol} and DLP (mGy) & (mGy.cm)	A	CT	Total
Willegaignon et al ²² (BR, 2015)	Brain/ Perfusion	-	^{99m} Tc-ECD	-	1203	-	8.17±1.69	-	-
	Brain/ Tumour	Tumour	²⁰¹ Tl-chloride	-	185	-	43.40±47.8	-	-
Alessio et al ¹⁹ (USA, 2015)	Bone		^{99m} Tc-MDP	1-4 (2.2±0.8) cases	999	-	-	-	-
Heart et al ²⁹ (UK, 2005)	Bone	-	^{99m} Tc-MDP	-	800	-	3	-	-
	Lung Perfusion	-	^{99m} Tc-MAA	-	100	-	0.3	-	-
	Myocardial	-	^{99m} Tc- tetrofosmin	-	400	-	3.1	-	-
	Myocardial	-	^{99m} Tc-sestamibi	-	400	-	3.7	-	-
	Myocardial	-	²⁰¹ Tl-chloride	-	80	-	12.9	-	-
	CBF	-	^{99m} Tc-Exam	-	500	-	4.8	-	-

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686 Note MIBG= metaiodobenzylguanidine, *= stress, H= hospital, MAA= macro aggregated albumin, ECD= ethyl cysteinate dimer, EXAM= Exametazime, Bone*= metastatic disease, equivocal uptake on
687 planar studies, characterisation of lytic and sclerotic lesions, localise and characterise site of unexplained pain, localise and characterise site of multifocal pathology, evaluation of new/persistent symptoms
688 following orthopaedic intervention, Post-thyroid ablation*= identify remnant thyroid tissues, and undertake accurate staging, Tumour MIBG*= Neuroendocrine tumour imaging, assessment of disease,
689 suitability for therapy and response, identification of primary tumours and metastases, assessment of post-therapeutic tumour targeting, and assessment of tumour recurrence, Octreotide*= Somatostatin
690 receptor imaging – assessment of disease, suitability for therapy and response, identification of primary tumours and metastases, assessment of post-therapeutic tumour targeting, and assessment of tumour
691 recurrence, Myocardial*= myocardial perfusion imaging and/or viability, and qualitative assessment of coronary calcium, CBF= cerebral blood flow.
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699 Table 4. Summary of hybrid NM/CT equipment.

Authors (Years & country)	Modality	Number	Manufacture	Year of installation	Type of detectors	
					Non-TOF	TOF
Kwon et al ¹⁵ (KR, 2016)	PET/CT	105	GE discovery (45): Discovery 600 (5), 690 (8), 710 (7), ST (4), STE (12), STE8(1), STE16(6), VCT(2) Philips (18): GXK6 (1), 16POWER (1), TF (4), TF16 (4), TF64 (8). Siemens (41): DUO (2), True Point (1), True point2 (2), True point6 (4), True point16 (2), True point 40 (12), True point64 (1), mCT20 (2), mCT40 (1), mCT 64 (5), mCT 128 (6), mCT X4R (1), mCT FLOW (2) No data (1)	2000-5 2006-10 2011-15 -	BGO (30) GSO (3) LBS (15) LSO (42)	LYSO (14) - - -
Jallow et al ²³ (US,2016)	PET/CT	158	GE (81) Philips (20) Siemens (56) Toshiba (1)	2001-2013 2004-2013 2003-2002 2005	- - - -	LYSO (158) - - -
Avramova-Cholakova et al ²⁴ (BU, 2015)	SPECT/CT	4	GE (1): Discovery NM/CT 670 with 16-detector row CT. Siemens (3): Symbia 2T (2) with a 2 detector CT row, Symbia T16 (1) with a 16 detector row CT	- - - -	- - - -	- - - -
Willegaignon et al ²² (BR, 2015)	PET/CT SPECT/CT	- -	GE (48%) Elscint (20%) Siemens (17%) Philips (12%) Other (3%)	- - - - -	- - - - -	- - - - -
Oliveira et al ²⁶ (BR, 2013)	PET/CT	42	GE (11) Philips(8) Siemens (20)	- - -	BGO (3) GSO (3) LSO (18) Nal (Ti) (2)	LYSO (2) - - -

701 Table 4. Summary of hybrid NM/CT equipment.

Authors (Years & country)	Modality	Number	Manufacture	Year of installation	Type of detectors	
					Non-TOF	TOF
Hart et al ²⁹ (UK, 2005)	PET/CT	7% (PET)	GE (4)	-	-	-
	SPECT/CT	75% (SPECT)	Siemens (3)	-	-	-
			GE (45%)	-	-	-
			Siemens (23%)	-	-	-
			Philips (25%)	-	-	-
			Park (0.8%)	-	-	-
			Toshiba (6%)	-	-	-
Mediso (0.4%)	-	-	-			
Brix et al ³⁰ (DE, 2002)	PET/CT	-	2 D and 3D PET equipment	-	-	-

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703 Note: GE= General electric, BGO= Bismuth germinate oxide, GSO= Gadolinium oxyorthosilicate, LBS= Lutetium based scintillators, LSO= Lutetium oxyorthosilicate, LYSO= Lutetium yttrium oxyorthosilicate, NaI

704 (TI)= Sodium iodide doped with thallium, and Min= Minutes.

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706 Figure 1. Flow diagram of included and excluded PET/CT and SPECT/CT NDRL studies.

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