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Nuclear medicine practice in Japan: a report of the seventh nationwide survey in 2012

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Abstract

Objective The Subcommittee on the Survey of Nuclear Medical Practice in Japan has performed a nationwide survey of nuclear medicine practice every 5 years since 1982 to survey current nuclear medicine practice and its changes over the years.

Methods The subcommittee sent questionnaires, including the number and category of examinations as well as the kind and dose of the radiopharmaceuticals during the 30 days of June 2012, to all of the nuclear medicine institutes. The total numbers for the year 2012 were then estimated.

Results A total of 1,167 facilities responded to the survey, including the 14 in vitro assay institutes and 266 PET centers. The recovery rate was 92%. The number of gamma cameras installed was 1,425 in total, with 9% decrease in 5 years. Dual-head cameras and hybrid SPECT/CT scanners accounted for 84% and 10.5%, respectively. The number of single-photon tracer studies in 2012 was 1.15 million which means decrease in 19% in 5 years and 29% in 10 years. All but cerebral perfusion study and sentinel lymphoscintigraphy have decreased. Bone scintigraphy was a leading examination (37%), followed by cardiac studies (28%) and cerebral perfusion study (18%) in order. SPECT studies showed an increase from 42% to 47%. PET centers have also increased from 212 to 295, as compared to the last survey. The 135 PET centers have installed one or two in-house cyclotrons. PET studies showed 26% increase in 5 years, with oncology accounting for 96%. ^{18}F -FDG accounted for

98% (505,990 examinations). PET examinations using ^{11}C -methionine have been increasing, with 3,352 examinations in 2012. The number of new PET studies using ^{11}C -PIB PET was 695. ^{131}I -radioiodine targeted therapies showed an increase, including 3,644 patients (54%) for thyroid cancer and 4,889 patients (18%) for hyperthyroidism. Out-patient thyroid bed ablation therapy with 30 mCi of ^{131}I accounted for 21% of cancer patients. The number of isolation rooms decreased from 158 to 135 in 5 years. In vitro radioassays have been declining continuously since 1992, with the number of studies of 9.0 million in 2012.

Conclusions Single-photon examinations showed a continuous tendency toward a decline in the survey. In contrast, the number of hybrid SPECT/CT scanner examinations has increased. PET/CT study in the oncology field and radionuclide targeted therapy have steadily increased.

Introduction

The Subcommittee on the Survey of Nuclear Medicine Practice in Japan, the Medical Science and Pharmaceutical Committee, the Japan Radioisotope Association (JRIA) has performed a nationwide survey of *in vivo* and *in vitro* nuclear medicine practice every 5 years since 1982 to provide beneficial information on the contemporary status of nuclear medicine practice in Japan [1-9]. The seventh survey was recently done in June 2012. A detailed comparison was performed between the survey and the previous surveys, analyzing the results.

Methods of survey

A sheet of questionnaire was sent to every institute, of which information JRIA has, to conduct clinical nuclear medicine examinations. The sheets included the survey items such as the numbers, the kinds, and injected doses of tracers in the nuclear medicine examination practice during the month of June in 2012. The categories of *in vivo* examinations using single-photon tracers were classified into brain or cerebrospinal fluid, salivary, thyroid, parathyroid, lung, heart or great vessels, liver or biliary tract, spleen or bone marrow, kidney or urinary tract, adrenal gland, bone or joint, gastrointestinal tract, tumor or inflammation, sentinel lymphoscintigraphy, other scintigraphy, and sample-counting examination.

To avoid counting twice the study number, the following was regarded as a single study: a study combined with another related study such as thyroid scintigraphy combined with thyroid

radioiodine uptake measurement; a study taking serial images such as radionuclide cisternography; a study in which the same radiopharmaceutical is injected twice within the same day such as stress and rest myocardial perfusion study using technetium-99m (^{99m}Tc)-labeled agents, and so on. All of the radiopharmaceuticals used, even if commercially available or unavailable, were recommended to be described in the questionnaire sheets.

The number and types of gamma cameras installed at each institute were also asked about. In addition, positron emission tomography (PET) and in vitro study, and radionuclide targeted therapy were included in the survey. The actual examination number and patients' number per year, performed or treated in 2012 were required to fill in the sheet with regard to PET study and radionuclide targeted therapy.

Regarding in vitro study, duplicated sample measurement was regarded as a single test, but serial sample measurements in a patient, such as overloading tests, were regarded as they were.

Results

The total number of institutes, of which information JRIA has as a nuclear medicine institute was 1,274 (Fig. 1). The breakdown is as follows: 1,170 institutes for in vivo single-photon study and/or radionuclide targeted therapy, and 295 for PET study. The former has decreased by 4.0% and the latter has increased by 39% in 5 years. The 15 institutes for in vitro study has markedly decreased by

69% in 5 years with a continuous decline since 1982. Of the 1,274 institutes to which the Subcommittee sent a sheet of questionnaire, 1,167 (91.6%) answered the sheet.

Figure 2 shows the number of the installed gamma cameras, which were obtained from the results of the respondents. A total of 1,425 gamma cameras were installed in 1,074 institutes (mean: 1.3 cameras). Dual-head cameras capable of SPECT acquisition accounted for 79% (Fig 3). The number of brand-new hybrid SPECT/CT scanners was 149. Of the 266 respondents with PET system, 108 have installed one or two cyclotrons, with a total number of 113 cyclotrons, meaning the increase of 5 centers installed with a cyclotron since 2007. The number of PET and hybrid PET/CT scanners was 374 in the 254 PET centers in the survey of the year, 2012, which means an increase in PET or PET/CT scanners by 75 for 5 years, as 299 in 192 PET centers in the survey of the year, 2007. The increase is ascribable to the development of the ^{18}F -FDG commercial deliver system during 5 years.

The estimated total number of single-photon tracer examinations in 2012 was 1.15 million, which means the number of administered radiopharmaceuticals. The result was found to be 18.9% decrease in single-photon tracer examinations when compared to that of the last survey in 2007 (Fig. 4). If the business days for nuclear medicine practice are assumed to be 250 days a year, approximately 4,600 studies were done nationwide per day. The categories of the single-photon studies are shown in Fig. 5. Bone scintigraphy was a leading examination (38.7%), followed by cardiovascular scintigraphy (29.4%) and cerebral SPECT study (18.5%) in order. The number of

cerebral SPECT study is stable in the past 15 years. Lymphoscintigraphy, of which sentinel lymphoscintigraphy accounted for 84.4%, increased, though the number was small yet. Overall, the number of single-tracer examinations except cerebral SPECT and lymphoscintigraphy has decreased, with more prominent decrease in tumor/inflammation scintigraphy.

Figure 6 shows chronological changes for each radiopharmaceutical from 1997 to 2012. ^{99m}Tc -HMDP was used most frequently for bone scintigraphy. Thallium-201 (^{201}Tl) chloride was mainly used for myocardial perfusion SPECT, of which 50.0% were carried out as electrocardiogram (ECG)-gated study. ^{99m}Tc -sestamibi and ^{99m}Tc -tetrofosmin were used less frequently, but 85.6% and 75.2% for ECG-gated study, respectively. Exercise or pharmacological stress test was applied to 69.0% of all of myocardial perfusion SPECT studies. The number of ^{123}I -MIBG myocardial scintigraphy has steadily increased. ^{123}I -IMP was most frequently used for cerebral perfusion SPECT, though ^{99m}Tc -ethylcystenatate dimer (ECD) was used with the similar frequency. Statistical parametric mapping was used in 75.6% of all of the cerebral perfusion SPECT with 15.6% increase, as compared to the data in 2007. ^{99m}Tc -galactosyl human serum albumin (GSA) was frequently used as a hepatobiliary imaging agent. The number of ^{99m}Tc -PMT and ^{99m}Tc -phytae studies has decreased prominently, but ^{99m}Tc -GSA studies minimally.

The total number of SPECT acquisition studies has decreased because the number of single-photon tracers has decreased. However, the percentage of SPECT acquisition has increased from 42.3% to 47.2% in 5 years. The percentage of each study is as follows: 77.3% for cerebral study,

67.4% for myocardial study, and 52.5% for tumor imaging study (Fig. 7).

PET studies were used mainly in oncology field, which accounted for 97.7% (Fig. 8). A total number of ^{18}F -FDG PET studies was 505,990, which accounted for 99.8% of all PET studies in 2012 and 25.5% increase as compared to the result in 2007. The use of a ^{13}N tracer was stable in these 10 years. Studies with an ^{11}C -positron emitter kept on increasing in these 15 years, though the total number remained small. The number of ^{15}O -PET studies has been apparently decreasing. ^{11}C -methionine and ^{13}N - NH_3 were major PET tracers other than ^{18}F -FDG. There was a striking increase in ^{11}C -methionine in these 10 years (Fig. 9). In addition, ^{11}C -PIB has been used frequently for the diagnosis of Alzheimer's disease in 5 years.

A total of 340 institutes have the facilities for radionuclide targeted therapy, which means the increase by 190 institutes as compared to the result in 2007. In contrast, the number of institutes running admission rooms for the therapy has decreased from 66 to 63, with the decrease in the admission rooms from 188 to 135 in 10 years. The numbers of patients with thyroid cancer or hyperthyroidism who underwent ^{131}I -targeted therapy, were 3,644 and 4,889, respectively, in the year from June 1st 2011 to June 30th 2012 (Fig. 10). Of all of the patients with hyperthyroidism, 77% were outpatients and underwent ^{131}I -radioiodine targeted therapy. Thyroid ablation therapy for outpatients using ^{131}I of 1,110 MBq, which was approved by the government in November 2010, was carried out in 764 patients (21.0%). Radionuclide targeted therapy for malignant neuroendocrine tumors using ^{131}I -metaiodobenzylguanidine (MIBG) was performed in 34 patients with an increase

by 14 patients as compared the results in 2007. The numbers of bone pain palliative therapy with ^{89}Sr and radionuclide targeted therapy for B-cell lymphoma with ^{90}Y -ibritumomab tiuxetan, which were approved by the government in 2007 and 2008, respectively, are shown in Fig. 10.

A total of 9.0 million in vitro radioassays were carried out in the year 2012. The number has been decreasing continuously since 1992. In this survey, tumor markers' radioassays were a leading group (14.9%), followed by the adrenal function tests' group (14.4%), and reno-vascular regulating function tests' group (9.2%) in order. By and large, the number of in vitro radioassays decreased, but the number of parathyroid function tests, adrenal function tests, ferrokinetics/hematopoietic tests, gonadotropic/placental function tests and cytokine measurements were almost stable in 5 years. The chronological changes in major tests in 30 years are shown in Table 1.

Discussion

The nationwide surveys have been repeatedly performed every five years and the current survey was the seventh one. It is estimated that marked changes in nuclear medicine practice have occurred because new radiopharmaceuticals and nuclear medicine equipment have devised almost every year. The current questionnaire survey was carefully prepared for comparing the results of previous surveys as accurately as possible before sending the questionnaire sheets to nuclear medicine institutes. For example, multiple studies done by a single administration of a

radiopharmaceutical were regarded as a single study to avoid counting twice or three times.

The number of facilities which utilize single-photon tracers and perform targeted radionuclide therapy declined for the first time since the surveys stated in 1982. The number of gamma cameras installed nationwide also declined. Consequently, the total number of single-photon tracer studies has been decreasing since 1997 when the fourth survey was conducted. The number of single-photon tracer examinations in 2012 was 1.5 million, which means a 19% and 29% decrease for 5 years and 10 years, respectively.

Bone scintigraphy remains a leading examination, accounting for approximately a third of all single-photon examinations. However, its application continues to decrease for 10 years. Single-photon scintigraphy for tumor detection has markedly decreased for 20 years. One reason for the decrease is explained by increase in use of ^{18}F -FDG PET, of which use was officially approved by the government, and covered by the national health insurance for ten types of malignancies in April 2002, and then an additional three types of malignancies in April 2006. Another reason might be explained by the development of other imaging modalities such as magnetic resonance imaging (MRI) or multi-detector row CT.

Cardiac scintigraphy (cardiovascular nuclear medicine) was the second leading examination. Contrary to the definite evidence of myocardial scintigraphy for evaluation of various cardiac diseases, its application to cardiac diseases has been decreasing for 10 years, suggesting the necessity to inform clinicians of the role cardiac scintigraphy plays in the clinical settings. The decrease in

ECG-gated blood pool cardiac imaging is clearly due to the increase in quantitative gated SPECT studies. ¹²³I-MIBG scintigraphy showed 1.4-fold increase. The main reason of the increase is explained by its use for the differential diagnosis among Parkinson disease, dementia of Lewy body disease, and parkinsonism, though the increase in patients with chronic heart disease may be attributable for the increase.

Slight increase was found in cerebral perfusion SPECT studies, likely due to clinical demand for the statistical image analysis in diagnosis of cerebral disorders, especially dementia.

Pulmonary, thyroid, renal (including dynamic study), liver, and bone marrow scintigraphy showed a decrease in the number of the studies, probably because of the development and nationwide spread of anatomical imaging modalities such as MRI, multi-detector row CT, and ultrasonography. The number of renal static scintigraphy did not change in 5 year, suggesting its clinical utility in detecting disease entities such as renal scar.

The number of adrenal studies was constant, probably because it has been established as a diagnostic tool for adrenal disorders. In other words, scintigraphy to evaluate specific organ function, which cannot be evaluated by other modalities, survives in the clinical practice of nuclear medicine.

What should be noted in changes of the recent trends for single-photon studies is steady increase in SPECT studies in all kinds of examinations, coupled with the increase in hybrid SPECT/CT scanners. Fusion images surely enhance reading performance of images and provide clinicians with more accurate information of the disease. Nuclear medicine specialists should

improve their reading skills by exploiting these state-of-art techniques.

The number of PET institutes and its studies dramatically increased just after the governmental approval of ^{18}F -FDG for the use of the oncologic use. The coverage of ^{18}F -FDG PET study by the national health insurance had started in Japan 2 months prior to the survey in 2002. Subsequently, the number of ^{18}F -FDG study increased as predicted at that time. In addition, a commercially available ^{18}F -FDG delivery system started in 2005, which also accelerated the use of ^{18}F -FDG studies. The current survey confirmed this trend for the increase in ^{18}F -FDG PET study. The number of ^{11}C -methionine studies has been steadily increasing in research work in oncology. In contrast, the number of ^{15}O -gas PET studies has decreased probably because it is laborious and wasteful to do the studies, though ^{15}O -gas PET study was approved by the government with a relatively low study cost and covered by the national health insurance in 1996.

Radionuclide targeted therapy for thyroid cancer has been increasing steadily since 1987. Radioiodine targeted therapy for hyperthyroidism showed a rapid increase in number after the publication of the guideline in 1998. The guideline says that patients are able to be released from an outpatient clinic if those receive 500 MBq of ^{131}I or less. In addition to the guideline publication, clinicians' preference and patients' demand are attributable to the increase in radioiodine targeted therapy for hyperthyroidism.

Patients with a high risk of recurrence after total thyroidectomy for differentiated thyroid cancer receive a benefit from the guideline of out-patient thyroid ablation published in 2010,

resulting in the timely application of thyroid ablation. However, the situation of ^{131}I targeted therapy has been deteriorating despite the increase in the patients with thyroid cancer, due to the shortage of the admission rooms and a long waiting time until admission.

The number of institutions conducting in vitro studies has been continuously decreasing over the past 30 years. The number of in vitro assays has decreased in all kinds of examinations except the examinations of samples with unstable substances or of complicated procedures. The trend toward the shift from radioassay to non-radioassay will continue even in the future. If most of in vitro radioassays will be concentrated to a few private laboratory centers, more careful and strict quality control should be required regarding radioassay in the future.

Conclusions

It was found out that nuclear medicine practice in Japan has kept on changing in the past 5 years. We are convinced that this survey report is useful in understanding the current status of the nuclear medicine practice and its future trend, and in devising the new strategy to strengthen a role nuclear medicine plays in the clinical setting and research work.

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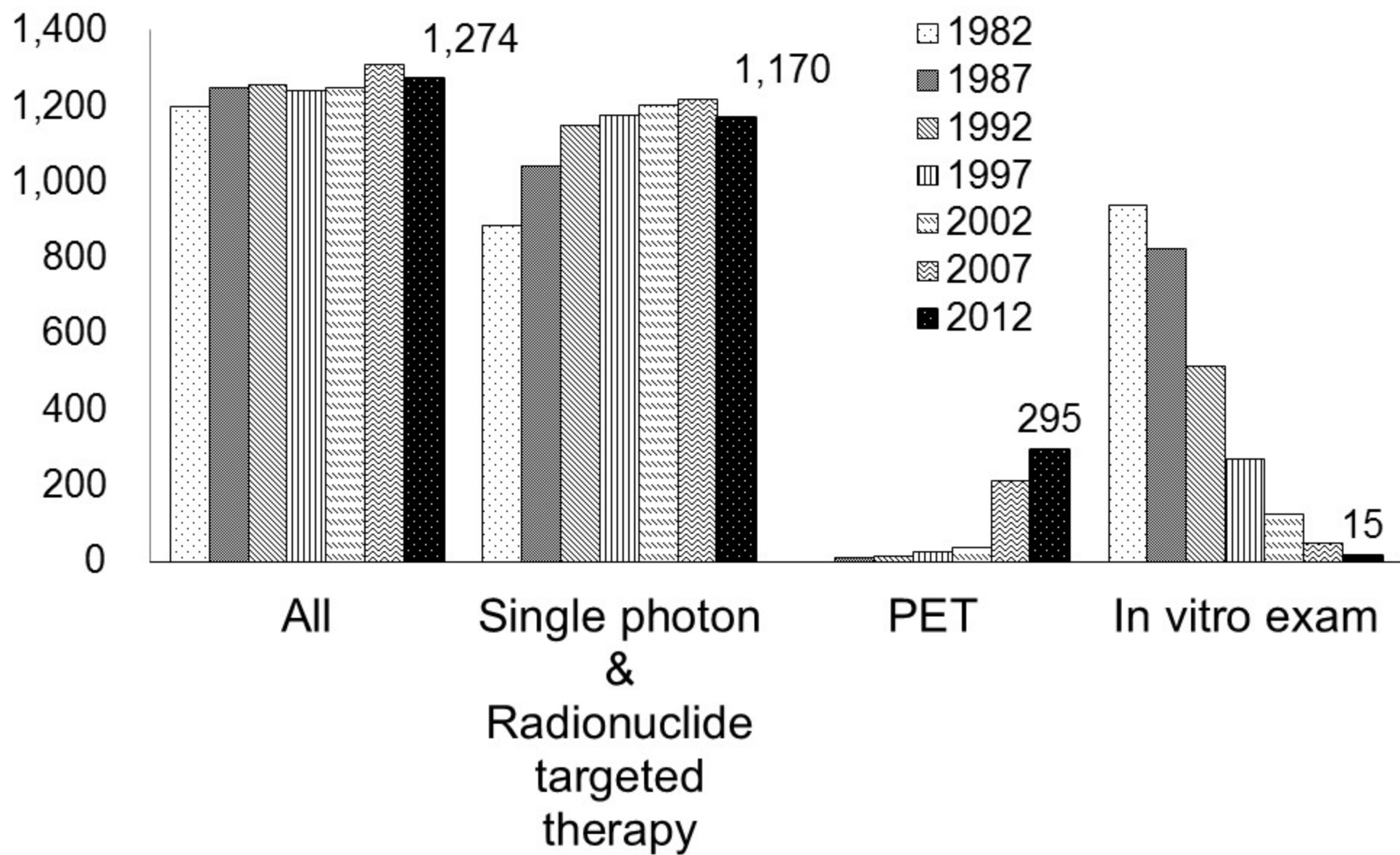
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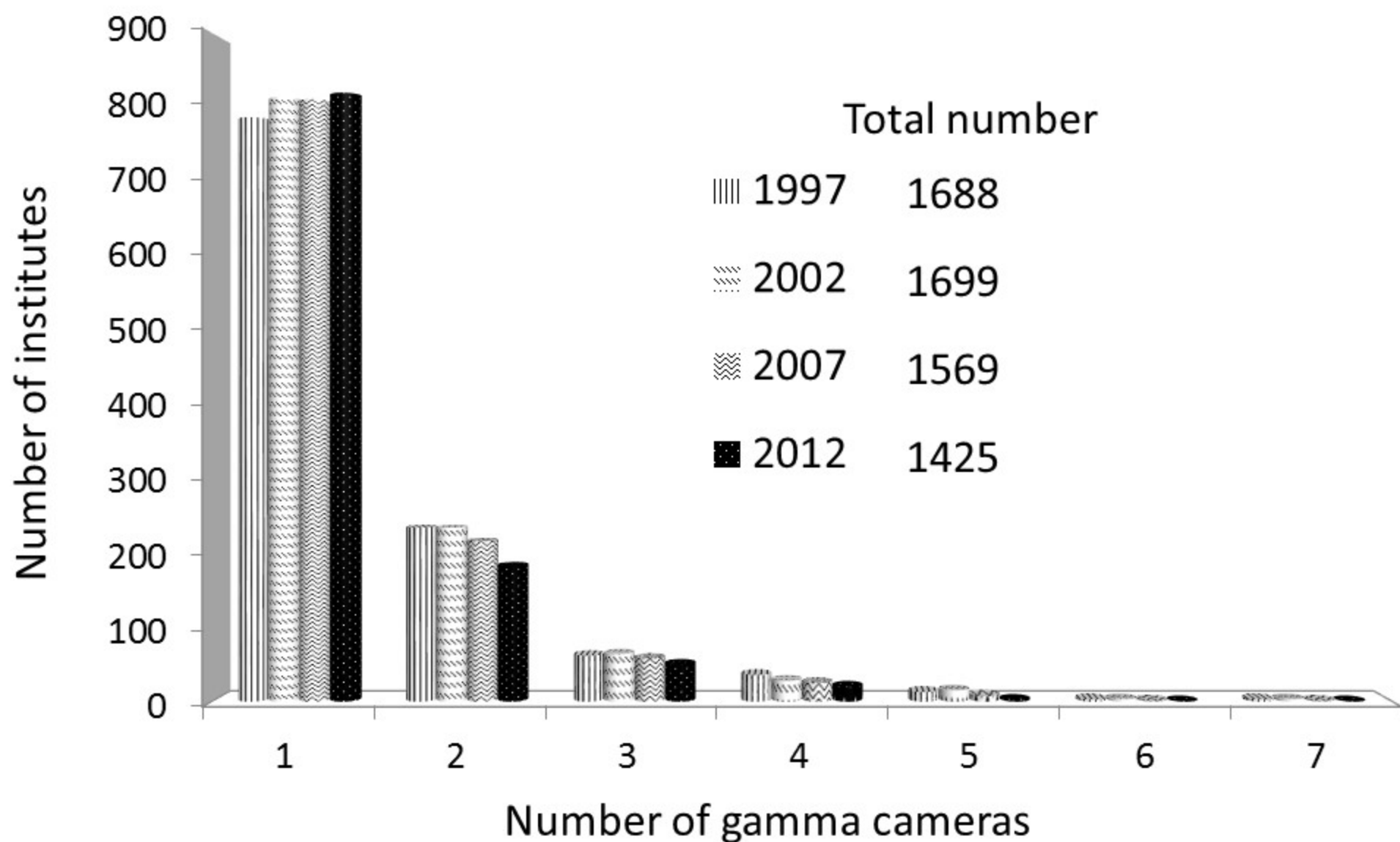
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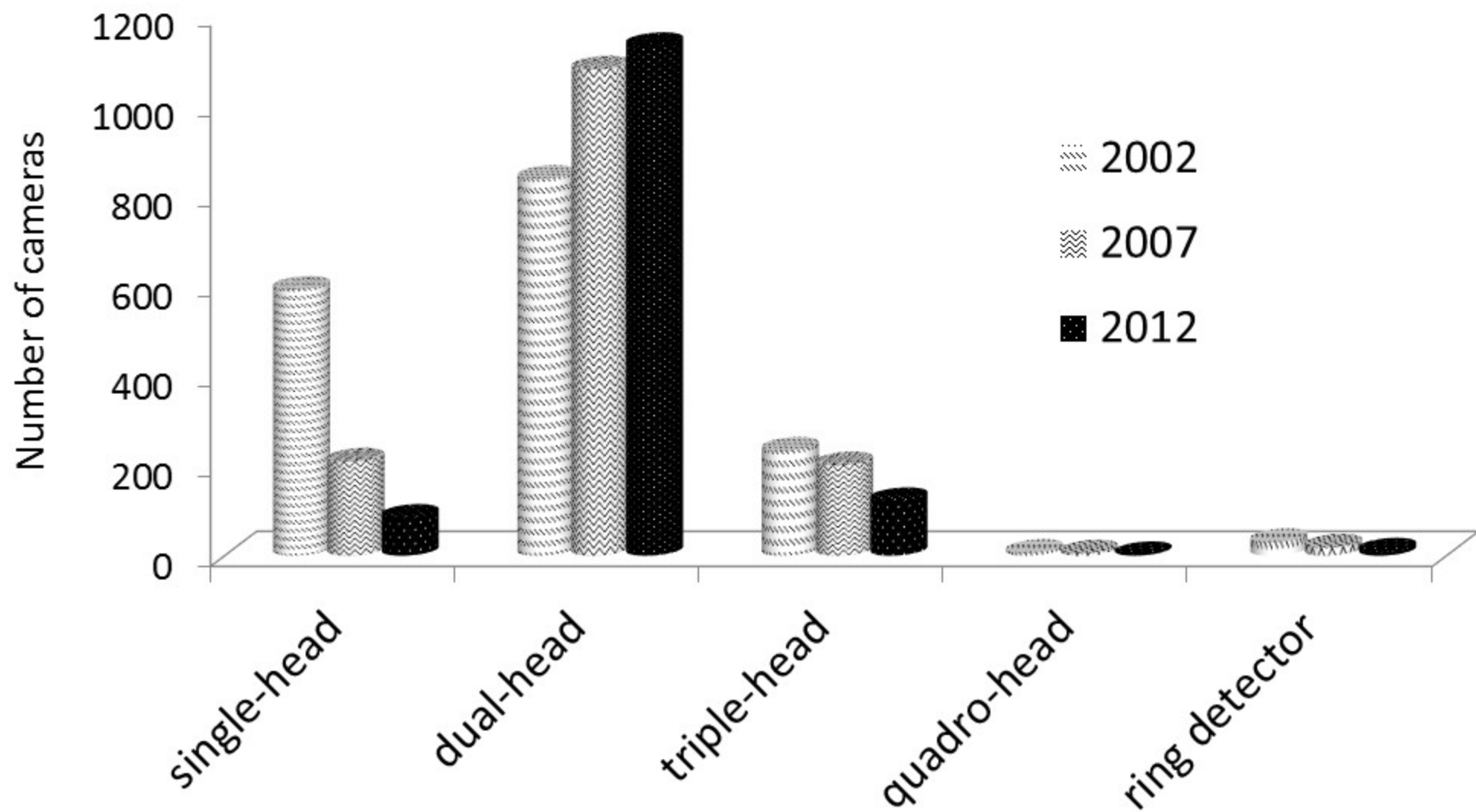
- Figure 1 Institutes conducting nuclear medicine practice
- Figure 2 Number of gamma camera installed in each facility
- Figure 3 Type of gamma camera
- Figure 4 Number of studies with single photon tracers performed in a year based on tracer administration
- Figure 5 Categories of single photon studies performed in a month
- Figure 6 Common radiopharmaceuticals in each category
- Figure 7 SPECT acquisition in each examination
- Figure 8 ^{18}F -labelled tracers used in a year
- Figure 9 Major positron tracers other than ^{18}F -FDG used in the survey year
- Figure 10 Number of radionuclide targeted therapy performed in the survey year

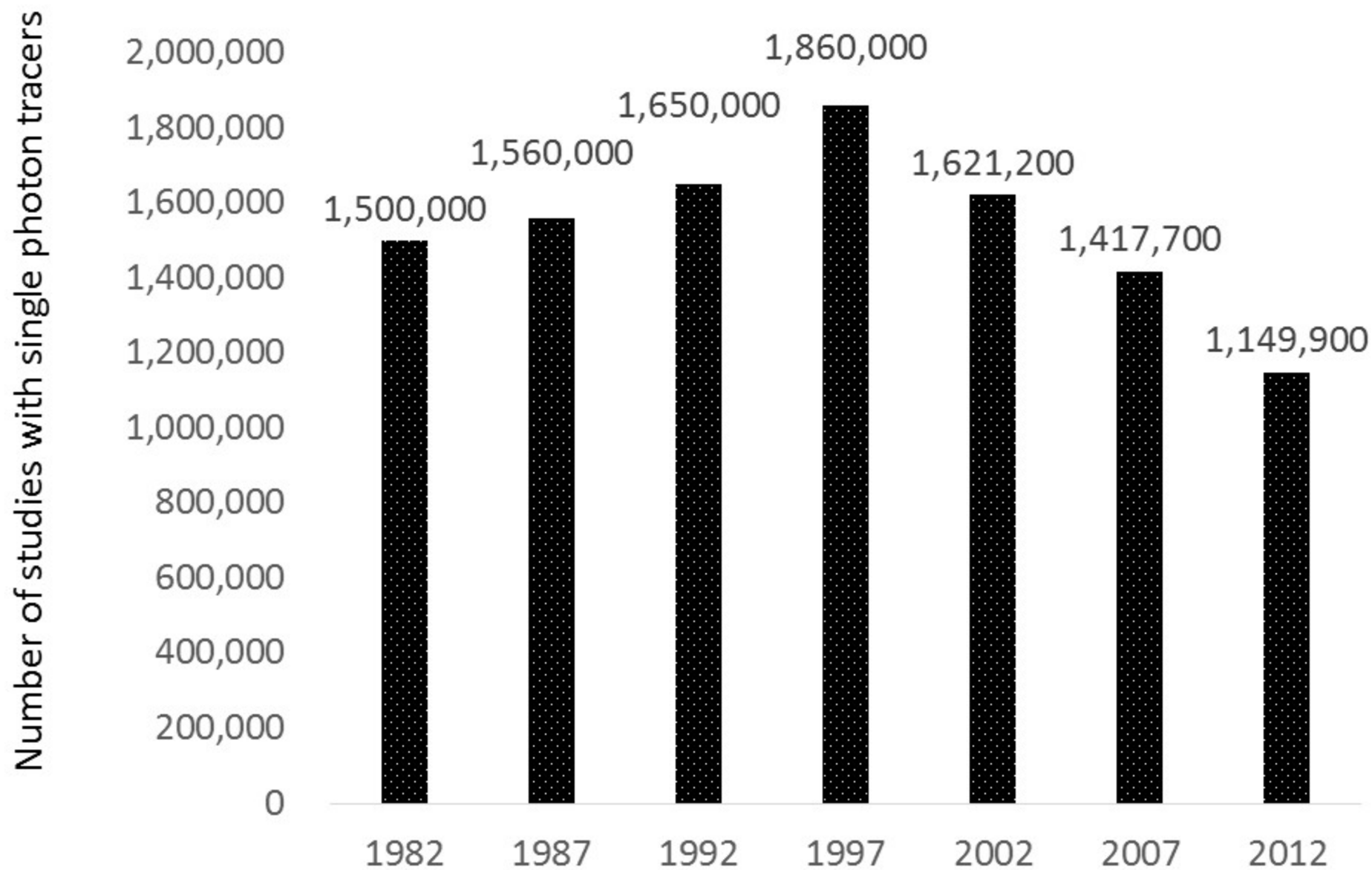
Table 1 Number and details of in vitro studies

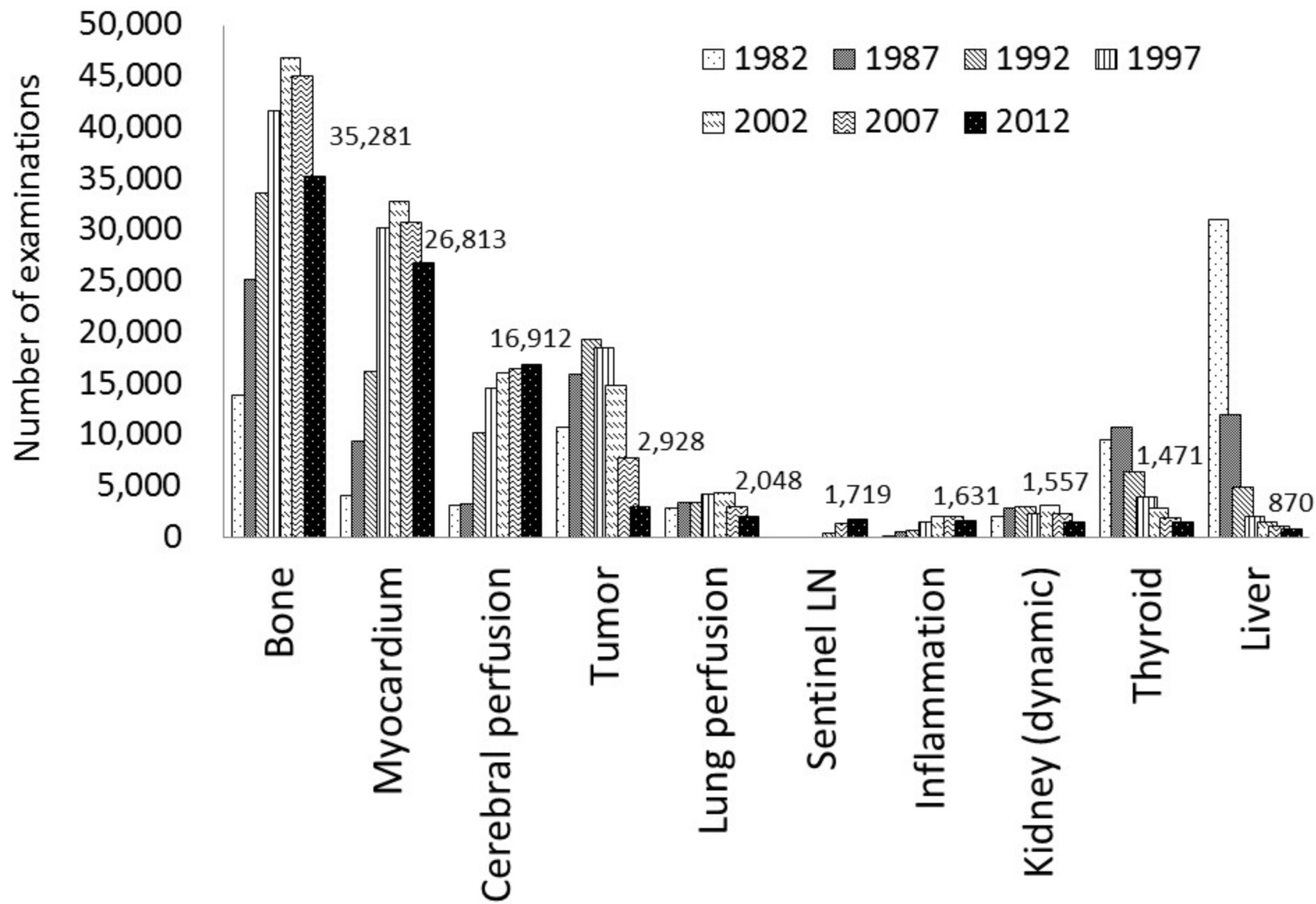
Year	1982	1987	1992	1997	2002	2007	2012	
Total number (x10 ⁶)	30.62	55.42	60.18	47.82	31.35	13.11	9.00	
Major study ranking	%	%	%	%	%	%	%	
1	CEA	11.7 CEA	9.6 CEA	7.3 CEA	7.9 HCV Ab	10.7 HCV Ab	6.7 Aldosteron	9.2
2	Insulin	9.6 Ige (RAST)	7.3 Ige (RAST)	5.7 HCV Ab	5.0 CA19-9	5.8 TSH-R-Ab	4.7 plasma renin activity	8.5
3	HBsAg	8.4 AFP	6.3 CA19-9	4.8 CA19-9	4.8 hBNP	5.4 Aldosteron	4.5 SLX	5.8
4	AFP	7.4 Insulin	5.8 TSH	4.6 Insulin	4.7 PA (PSA)	4.6 plasma renin activity	4.3 anti-DNA Ab	5.6
5	T4	6.4 HBsAg	5.5 Insulin	4.0 TSH	4.1 CEA	4.5 hANP	4.3 anti-GAD Ab	5.1
6	TSH	5.7 beta2-microglobulin	4.8 AFP	3.8 AFP	4.0 Insulin	3.7 Tg	4.3 TIBC	4.6
7	HBsAb	5.5 CA19-9	4.5 FT4	3.6 FT4	3.5 SCC	3.0 Tg Ab	4.1 Cortisol	4.5
8	T3	5.5 TSH	3.9 HBsAg	3.4 FT3	3.1 CA125	2.8 SCC	3.6 I-CTP	4.4
9	beta2-microglobulin	5.1 T4	3.8 beta2-microglobulin	3.3 C-peptide	2.6 iPTH	2.4 TPO Ab	3.6 IGF-1	3.4
10	Ige (RAST)	3.6 T3	3.8 Ferritin	3.1 HBsAg	2.5 AFP	2.2 ACTH	3.5 TRAb	3.1











1997
 2002
 2007
 2012

