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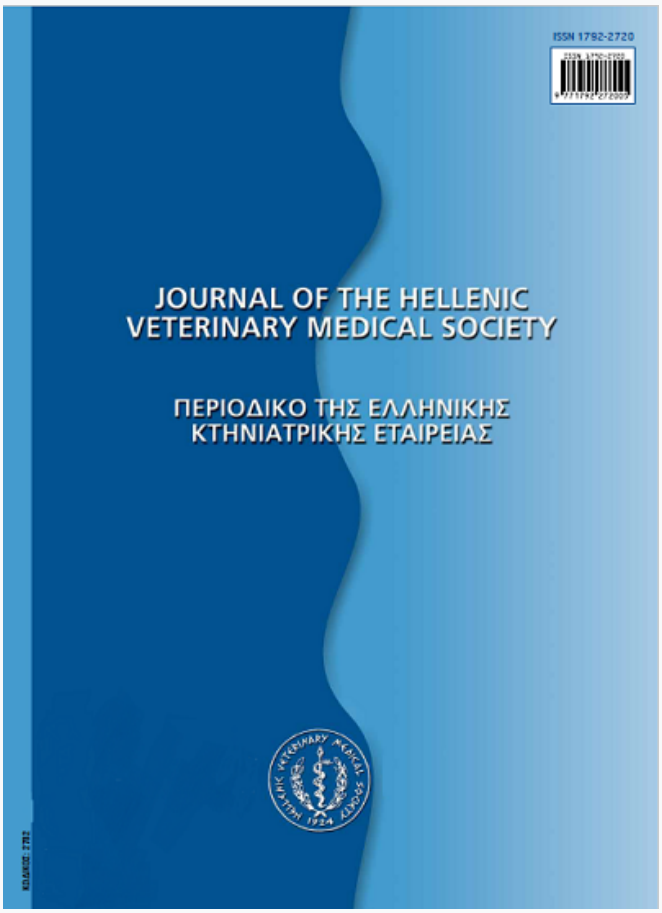

The contribution of laboratory animals to diagnostic imaging research in Greece

S. TSELEPIDIS, K. VASSIOU, D. ARVANITIS, C. KALOGEROPOULOU, K. MARINOU

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Review article
Ανασκόπηση

The contribution of laboratory animals to diagnostic imaging research in Greece

Tselepidis S[1]., Vassiou K[2]., Arvanitis D[2]., Kalogeropoulou C[3]., Marinou K[4].

[1]*Military Veterinary Hospital and Training Center KENOK, 41334 Larissa, Greece.*
[2]*Department of Anatomy, Faculty of Medicine, University of Thessaly, 1400 Larissa, Greece.*
[3]*Department of Radiology, Department of Medicine, University of Patras, 26504, Patras, Greece.*
[4]*Ministry of Rural Development and Food, Department of Animal Welfare, 10176 Athens, Greece.*

Η συμβολή των ζώων εργαστηρίου στην πρόοδο της ακτινολογικής έρευνας στην Ελλάδα

Τσελεπίδης Σ[1]., Βάσσιου Κ[2]., Αρβανίτης Δ[2]., Καλογεροπούλου Χ[3]., Μαρίνου Κ[4].

[1]*Στρατιωτικό Κέντρο Εκπαίδευσης και Νοσηλείας Κτηνιατρικού ΚΕΝΟΚ, 41334 Λάρισα.*
[2]*Εργαστήριο Ανατομίας, Τμήμα Ιατρικής, Πανεπιστήμιο Θεσσαλίας, 1400 Λάρισα.*
[3]*Εργαστήριο Ακτινολογίας, Τμήμα Ιατρικής, Πανεπιστήμιο Πάτρας, 26504, Πάτρα.*
[4]*Υπουργείο Αγροτικής Ανάπτυξης και Τροφίμων, Τμήμα Προστασίας των Ζώων , 10176 Αθήνα.*

ABSTRACT. Biomedical research in Greece has rapidly developed during the last 30 years. Diagnostic imaging groundwork is a significant field of interest which has been developed by taking advantage of the basic and applied research capacities including the use of small and large animal models, conventional and/or genetically modified ones. This important outbreak in research has been enhanced by the construction of modern facilities in universities, medical and other academic research centers, the use of new advanced installed equipment, modern imaging techniques, specific contrast media and, of course, specialized personnel. In this manuscript, the research performed regarding diagnostic imaging techniques using animal models in Greece since 1983 is presented. More specifically a recording of the Greek research centers, the number of researchers, species and figures of animal models, diagnostic imaging techniques used, as well as the contribution of projects in the evolution of diagnostic imaging in medicine and veterinary science is presented.
Keywords: *laboratory animals, imaging, research, Greece*

Postal and electronic addresses of the corresponding author:
Tselepidis Stavros, 57 Farsalon Str. Larissa,
Greece, postal code 41335
e-mail : stselepidis@hotmail.com

Τσελεπίδης Σταύρος, Φαρσάλων 57 Λάρισα,
ΤΚ 41335 Τηλ. +306972557239,
e-mail : stselepidis@hotmail.com

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Περίληψη. Η έρευνα όσον αφορά τις βιοϊατρικές επιστήμες στον ελλαδικό χώρο παρουσίασε την τελευταία τριακονταετία αλματώδη αύξηση. Ειδικότερα η ακτινολογική έρευνητική δραστηριότητα αναπτύχθηκε αξιοποιώντας τις δυνατότητες που προκύπτουν σε επίπεδο βασικής και εφαρμοσμένης έρευνας από την χρήση μικρών και μεγάλων ζωικών προτύπων, συμβατικών ή/ και γενετικά τροποποιημένων. Στο γεγονός αυτό συνέβαλε και η αξιοποίηση των νέων προηγμένων υποδομών για έρευνα των νοσηλευτικών και ακαδημαϊκών ιδρυμάτων, οι νέες τεχνολογίες απεικόνισης, η χρήση ειδικών σκιαγραφικών ουσιών αλλά και το εξειδικευμένο προσωπικό. Στην παρούσα εργασία περιγράφεται κατα το δυνατον το σύνολο του ακτινολογικού ερευνητικού έργου που έχει πραγματοποιηθεί στην Ελλάδα από το 1983 με τη χρήση ζωικών προτύπων. Συγκεκριμένα καταγράφονται τα ερευνητικά κέντρα, ο αριθμός των επιστημόνων, ο αριθμός και το είδος των ζωικών προτύπων, οι απεικονιστικές μέθοδοι που χρησιμοποιήθηκαν, καθώς και η συμβολή της ερευνητικής προσπάθειας στην εξέλιξη των απεικονιστικών μεθόδων στη ιατρική του ανθρώπου και των ζώων.
Λέξεις κλειδιά: *ζώα εργαστηρίου, απεικόνιση, έρευνα, Ελλάδα*

INTRODUCTION

Scientific research in Greece has steadily developed in all fields, especially, since the 1950s despite financial or bureaucratic restraints observed throughout the years. As far as biomedical research is concerned, all advances in the last decades have been achieved not only due to clinical observations, recordings and clinical trials but also due to experimental studies with the appropriate background, facilities and reinforcement with appropriately educated and trained personnel. The scientific progress obtained with the use of small or large sized, conventional and/or genetically modified animal models is outstanding.

A significant percentage of research advances has been accomplished with the use of diagnostic imaging technology in animals used for scientific purposes. Both anatomical and functional information may be gathered by its application, as well as by the use of contrast agents and specific test substances. Another aspect that should be considered while investigating diagnostic imaging studies is their contribution to laboratory animal science itself with the timely diagnosis and recording of precise humane endpoints (Brønstad and Dontas, 2011).

Diagnostic imaging research in Greece has been increasing tremendously during the last 30 years following the aforementioned scientific evolution and taking advantage of all technological and functional possibilities that live animals may offer in the context of basic and applied research (Balta, 2006). The first recorded radiographic research in Greece, in which dogs were used as experimental models, was a significant part of a PhD thesis carried out in the National and Kapodistrian University of Athens School of Medicine and dealt with the pathogenesis of the intermittent claudication syndrome of the knee joint (Gyftokostas, 1983).

It should be stressed that research facilities mentioned in this manuscript are registered as user, breeding and/or supplying establishments for animals used for experimental purposes according to applicable European and National legislation and fully comply with the requirements of the relevant Presidential Decree (PD 56/2013 (Governmental Gazette A' 106) which transforms the European Directive 2010/63/EC "on the protection of animals used for scientific purposes" (Official Journal of the European Union L 276) into Greek Law forming the official current national legislation). Furthermore, all the research establishments apply the guidelines issued by international federations and scientific associations such as the Federation of European Laboratory Animal Science Associations - FELASA and the International Council of Laboratory Animal Science - ICLAS, whereas they routinely implement programs of veterinary care (preventive and clinical veterinary medicine) and health monitoring schemes. (Voipio et al., 2008).

The research performed regarding diagnostic imaging techniques using animal models in Greece since 1983 to 2014 is described. More specifically Greek research centers, the number of researchers involved, species and numbers of animal models, diagnostic imaging techniques used, as well as the contribution of projects in the evolution of diagnostic imaging in medicine and veterinary science is presented.

Materials and methods

In the present study we looked into national and

Table 1. Demographic data of the research protocols that have used laboratory animals for diagnostic imaging research purposes in Greece since 1983.

Universities	National and Kapodistrian University of Athens	Aristotle University of Thessaloniki	University of Patras	University of Ioannina	University of Crete	University of Thessaly	University of Thrace
Number of University departments	2	3	1	2	3	2	1
Number of Laboratories and Medical Clinics	9	10	5	3	4	9	1
Number of projects	34	44	12	9	12	19	2
Researchers number	180	200	95	42	58	117	14
Animal model species	Rabbits Rats Pigs Mouse Dogs	Rabbits Rats Pigs Small ruminants Dogs Horses Cats	Rabbits Rats Pigs Small ruminants Hens	Rabbits Rats Small ruminants Dogs	Rabbits Mice Monkeys Rats	Rabbits Rats Pigs Small ruminants Dogs	Rabbits Rats
Number of animals	727	864	446	257	132	427	70
End of project	Euthanasia 22 Survived 12	Euthanasia 16 Survived 32	Euthanasia 5 Survived 7	Euthanasia 7 Survived 2	Euthanasia 4 Survived 8	Euthanasia 7 Survived 12	Euthanasia 1 Survived 1

international digital scientific databases, in order to retrieve the most relevant publications available, that present scientific protocols with the use of animals in diagnostic imaging research in Greece since 1983 until 2014. More specifically, the national database of Greek PhD theses of the National Documentation Database (http://www.didaktorika.gr/eadd/), the Hellenic Academic Libraries link, (http://www.heal-link.gr/), as well as the PubMed database of MEDLINE, which belongs to the US National Library of Medicine, were chosen. Four hundred (400) publications were studied, out of which one hundred and five (105) original research publications and twenty-six (26) PhD theses with diagnostic imaging research on various animal models were further processed.

Experimental protocols on animals with the use of diagnostic imaging techniques have been performed in most academic schools of Health Sciences in Greek universities as well as the Agricultural University of Athens. These Schools include two Schools and five Departments of Medicine in the universities of Athens, Thessaloniki, Patras (University of Patras), Ioannina (University of Ioannina), Herakleion (University of Crete), Larisa (University of Thessaly), Alexandroupolis (Demokretian University of Thrace) , the School of Dentistry in Athens, the Department of Dentistry in Thessaloniki and two Departments of Veterinary Medicine in Thessaloniki and Karditsa (University of Thessaly) respectively. Furthermore, recently developed experimental and research institutes in Greece have tremendously contributed to the diagnostic imaging research with the use of animals such as the Biomedical Research Foundation of the Academy of Athens, the Biomedical Sciences Research Center "Alexander Fleming", the Laboratory Animals" facility of the Hellenic Pasteur Institute, the National Center for Scientific Research "Demokritos" – all based in Athens, the Research – Experimental Centre of the "Papageorgiou" General Hospital in Thessaloniki etc., as well as private research centers such as the Experimental and Research Centre of ELPEN Pharmaceutical Company in Athens.

Twenty-six diagnostic imaging techniques were used in total and are divided into routine and original

Table 2. Imaging techniques used in research protocols with laboratory animals for diagnostic imaging research purposes in Greece since 1983.

Universities	National and Kapodistrian University of Athens	Aristotle University of Thessaloniki	University of Patras	University of Ioannina	University of Crete	University of Thessaly	University of Thrace
Administration of drugs or contrast media	14	12	6	0	7	4	0
Clinical case	0	17	0	6	0	5	0
Research project	34	27	12	3	12	14	2
Diagnostic imaging technique	Ultrasonography Computed tomography Magnetic resonance imaging Peripheral computed tomography Radiography Lymphography Positron emission tomography–computed tomography PET/CT Bone density measurement	Radiology 3D-CT Cephalometic analysis Ultrasonography Computed tomography Magnetic resonance imaging Myelography Lymphography	Ultrasonography Computed tomography Magnetic resonance imaging Optical coherence tomography Digital subtraction angiography Intraoperative intravenous urography Digital angiography Radioscopy	Ultrasonography Fluoroscopy Intravascular Ultrasonography Computed tomography Magnetic resonance imaging Angiography Lymphography Micro-computed tomography Synchroton radiation microtomography	Ultrasonography Computed tomography Magnetic resonance imaging Optical coherence tomography Quantitative autoradiographic method Noncontact fluorescence molecular tomography	Radiology Angiography Ultrasonography Computed tomography Positron emission tomography	Ultrasonog-raphy Computed tomography
PhD theses	11	11	2	1	0	1	0
Collaboration with Greek Educational Organisations	3	2	1	0	0	0	0
Collaboration with Foreign Educa-tional Organisations	6	2	2	0	0	1	0

experimental techniques. Routine techniques included radiography, angiography, diagnostic ultrasonography, computed tomography, magnetic resonance imaging, digital subtraction angiography, transcranial color-coded-Doppler ultrasonography, myelography, lymphography, fluoroscopy, bone density measurement and radioscopy. Original experimental diagnostic techniques applied included positron emission tomography–computed tomography, 3D-CT cephalometic analysis, optical coherence tomography, frequency domain optical coherence tomography, quantitative autoradiographic method, peripheral quantitative computed tomography, noncontact fluorescence molecular tomography, intravascular ultrasonograpy, micro-computed tomography, synchroton radiation microtomography, intraoperative intravenous urography, quantitative computed tomography, gamma-ray photon absorptiometry and image directed doppler tomography.

Results

From data recorded and presented in Tables 1 and 2 it is deducted that 3,534 laboratory animals in total have been used in protocols with diagnostic imaging techniques since 1983 until 2014. Ten (10) different animal model species were used in all these experimental protocols, out of which most were rodents. More specifically, 1025 rats *(Wistar),* 73 mice, 1093 rabbits *(New Zealand White),* 110 minipigs, 248 small ruminants (sheep and goats), 770 dogs *(Beagle),* 196 Common European Cats, 6 Rhesus macaques (*Macaca mulatta)*, 12 hens and 1 horse have been recorded. Forty-four percent (44%) of the experimental protocols (57 out of 131) were terminal-stage for the animals. More specifically, 1946 animals were euthanized according to the provisions of the applicable legislation according to the research period, since this procedure was necessary in order to extract objective data from the experimental protocols.

Most animals (1120 in total), were used in the Aristotle University of Thessaloniki. One thousand and one hundred seventeen (1117) animals have been used by the National and Kapodistrian University of Athens', 446 animals by the University of Patras, 402 animals by the University of Thessaly, 257 animals by the University of Ioannina, 70 animals by the University of Thrace and 122 animals by the University of Crete during this period.

Thirty-four (34) experimental protocols including diagnostic imaging research have been performed in Athens and more specifically in the faculties of the National and Kapodistrian University of Athens and the Agricultural University of Athens. Two of these protocols were performed with the collaboration of five USA and Saudi Arabian academic institutions. Five clinics of the University of Athens School of Medicine and four laboratories of all Athens Faculties with eighty (80) Greek and international researchers worked on these protocols.

The relevant experimental protocols were performed in the user establishments of the University of Athens School of Medicine and six university hospitals that belong to it, the University of Athens School of Dentistry, the University of Athens Department of Biology and the Agricultural University of Athens and two research centers, the Experimental and research Centre of ELPEN Pharmaceutical Company and the National Center for Scientific Research "Demokritos"). Two experimental protocols were accomplished from the Center of Experimental Surgery of the Biomedical research Foundation of the Academy of Athens exclusively, one of which was performed in collaboration with a USA research institute and where seven (7) Greek and three (3) foreign researchers participated. The scientific work produced in all the above mentioned establishments led to publications in peer reviewed journals and eleven (11) PhD theses, out of which ten (10) have been issued by the School of Medicine and one by the School of Dentistry.

Forty-four (44) experimental protocols have been performed in the Aristotle University of Thessaloniki that consist the largest number in total of diagnostic imaging research experimental protocols performed in the country. Two of these protocols were conducted with the collaboration of two university faculties of the UK and USA respectively. One more experimental protocol was in collaboration with the University of Thessaly in Greece. A total of three clinical departments of the Aristotle University of Thessaloniki Department of Medicine including four laboratories of all Thessaloniki Departments of the School of Health Sciences with two hundred Greek and foreign researchers worked on these protocols. The relevant experimental protocols were performed in the user establishments of the University of Thessaloniki Department of Medicine and two hospitals "Papageorgiou" and the 424 General Military Hospital. The scientific work produced in all the above mentioned establishments led to publications in peer reviewed journals and eleven (11) PhD theses, out of which three from the Department of Medicine, four from the Department of Veterinary

Medicine and four from the Department of Dentistry.

Twelve (12) experimental protocols have been performed in the University of Patras with the use of diagnostic imaging techniques, three of which were performed in collaboration with academic institutions based in USA and Israel, as well as with the Technological Educational Institute of Athens. Five in total clinics and laboratories of the University of Patras Department of Medicine with ninety-five Greek and international researchers worked on these protocols. The relevant experimental protocols were performed in the user establishments of the University of Patras Department of Medicine. The scientific work produced in all the above mentioned establishments led to publications in peer reviwed journals plus the presentation of two PhD theses from the Department of Medicine.

Nine (9) experimental protocols have been performed in the University of Ioannina with the use of diagnostic imaging techniques. Three in total clinics of the University of Ioannina Department of Medicine including laboratories of the Department of Materials and Engineering with forty-two Greek researchers worked on these protocols. The relevant experimental protocols were performed in the user establishments of the University of Ioannina Department of Medicine and the Department of Materials and Engineering respectively.

The scientific work produced in all the above mentioned establishments led to publications in peer reviewed journals and one PhD thesis from the Department of Medicine.

Twelve (12) experimental protocols have been performed in the School of Medicine of the University of Crete with the use of diagnostic imaging techniques. Four in total clinics and laboratories of the University of Crete School of Medicine with forty-nine Greek researchers worked on these protocols. One experimental protocol has been performed in the Department of Laser of the Technological Educational Institute of Crete and nine Greek researchers worked on this protocol (Garofalakis et al., 2007).

Eighteen (18) experimental protocols have been performed in the University of Thessaly with the use of diagnostic imaging techniques, one of which was performed in collaboration with an academic institution based in the UK. Seven in total clinics of the University of Thessaly School of Health Sciences including two laboratories with one hundred and seven Greek and foreign researchers worked on these protocols. The relevant experimental protocols were performed in the user establishments of the University of Thessaly Medical and Veterinary Department respectively. The scientific work produced in all the above mentioned establishments led to the presentation of scientific publications plus one (1) PhD thesis from the Department of Medicine.

Two (2) experimental protocols have been accomplished in the Laboratory of Experimental Surgery and Surgical Research, Department of Medicine, Democritus University of Thrace, Alexandroupolis, Greece. Fourteen Greek researchers worked on these protocols (Ypsilantis et al., 2007, 2009).

In summary, the field of the diagnostic imaging research performed in animal models in the above mentioned publications can be divided as follows: Out of the one hundred and thirty one (131) protocols, thirty-five (35) referred to new medical treatments, seventeen (17) to merely diagnostic purposes, thirteen (13) to surgical treatments, twelve (12) to dentistry protocols, eleven (11) to the anatomical investigation of animals themselves, nine (9) to the mapping of organs and anatomical structures of laboratory animals, nine (9) to cancer research, five (5) to the improvement of contrast media, five (5) to the investigation of the lymphatic system, nine (9) to the investigation of the locomotive system, three (3) to the optimization of vascular imaging, two (2) to (early) pregnancy diagnosis, and one (1) to the development of diagnostic techniques for the eye .

Discussion

To our knowledge, one hundred and thirty one (131) studies using live animals have been performed since 1983 in Greece with the use of diagnostic imaging techniques applied on experimental basis, as well as established ones and therefore routinely used. These trials had the scope of evolving and confirming the capacities of an experimentally developed diagnostic imaging technique, or to contribute to the diagnosis of various diseases or conditions. The impressive rise in the number of trials using live animals in Greece can be also attributed to the fact that many new academic establishments were founded in various prefectures and were staffed with capable and well trained scientific and technical personnel and the relevant technical equipment. Further on, the foundation of new university faculties and departments (medical, veterinary and biology departments) with the simultaneous design of animal user establishments has contributed to this result.

The outcomes of a significant percentage of experimental studies that took place in Greek research centers as mentioned in the previous sections have significantly contributed to the evolution of diagnostic imaging protocols regarding the technical advance of methods themselves and their implementation in the diagnostic approaches of various diseases and abnormalities. The relevant PhD theses in Greece provided with important useful data.

The use of X-rays in the healing process of traumas after tooth extractions in dentistry was effective in rats in an attempt to investigate whether this could potentially apply to humans as well (Papadakis, 1995).

In projects with the use of rabbits it was shown that the use of carbon dioxide as contrast medium in digital subtraction angiographies has more beneficial effects compared to iodine-based contrast agents, because it minimizes allergic reactions or chronic renal failure (Dimakakos, 2006). Another project in cats confirmed the absence of postmyelographic adverse effects and high radiographic resolution of the contrast medium iotrolan when used in cervical myelography tests (Patsikas et al, 1999).

In projects where rabbits, mice, but also mere tissues, such as chorioallantoic membranes were used (Karnabatidis, 2001), new techniques as non-contact fluorescence molecular tomography and digital subtraction angiography and biocompatible contrast media (water for injection with gadopentetate dimeglumine solution) that upgrade imaging results in special organs (e.g. ear) were tested and evolved (Maris et al., 2002), (Garofalakis et al., 2007), (Stasinopoulou et al., 2014).

In various studies with different animal model species (rabbits, dogs and cats) the lymphatic system was investigated with the use of various diagnostic imaging techniques including original ones such as MRI lymphography performed at a research level (Dimakakos et al, 1998). Furthermore, diagnostic imaging techniques (e.g. ie. angiography) have significantly contributed to the scientific interpretation of physiologic mechanisms of the locomotive system (Savaki et al, 1999, Raos et al, 2014), as well as the impact of invasive surgical methods to the male genital system (Gouletsou et al, 2008).

Early diagnosis of pregnancy is a common request of all clinicians and researchers, so the publication of an atlas of ultrasonographic diagnosis, confirmation and evaluation of all stages of rat pregnancy has substantially contributed to the reduction of laboratory animals sacrificed in reproduction according to the 3R principle projects (Ypsilantis et al., 2009), (Stasinopoulou et al., 2014).

In various projects mapping of organs and anatomical structures of laboratory animals was successfully performed, such as the *vasa vasorum* in pigs (Sokolis et al., 2002), the aorta and coronary arteries in pigs and sheep (Bourantas et al., 2005), (Vavuranakis et al., 2007), the visceral vessels in rats (Kalogeropoulou, 1998), the skin in dogs (Mantis et al., 2014), the testicles in rams and dogs (Gouletsou et al., 2003), (Gouletsou et al., 2008), the lymphatic system in dogs (Patsikas et al., 1996), (Patsikas, 1992) and cats (Papadopoulou, 2008) the lymphatic system of normal and neoplastic mammary glands in dogs (Patsikas et al., 2006), the skull in sheep (Papadopoulos et al., 2005), (Papadopoulos et al., 2006), with experimental diagnostic imaging techniques such as contrast-enhanced intracoronary ultrasonography, transcranial color-coded-Doppler ultrasonography, (14) C-deoxyglucose imaging (Gregoriou et al., 2005), synchrotron micro-CT (Tzaphlidou et al., 2006), X-ray absorptiometry (Tzaphlidou et al., 2000), 3D reconstruction using biplane angiography, intravascular ultrasound images and gamma-ray photon absorptiometry (Fountos et al., 1997).

Other projects led to the better imaging and early cancer diagnosis via original (Polizopoulou et al, 2004), (Patsikas et al., 2006) and modern imaging techniques as Quantum dots-bevacizumab (Gazouli et al., 2014) and digital subtraction angiography (Karnabatidis, 2001).

The optimization of vascular imaging with the use of digital techniques is a constant research goal as well as the performance of various relevant projects with the use of laboratory animals. Studies where new user friendly computed models of digital subtraction angiography in the University of Patras have been accomplished and their outcomes are ready to be further used in other experimental and clinical trials (Kagadis et al., 2008). Furthermore, new diagnostic imaging techniques of the eye (Shear-wave ultrasound elastography) are expected to contribute to the precise and early diagnosis of its anatomical abnormalities (Detorakis et al., 2014), whereas original techniques have been used at the last stage of invasive technique studies such as stenting (Kitrou et al., 2014), (Kasapas et al., 2014).

In addition, projects with the use of various diagnostic imaging techniques (ultrasonography, MRI) were used for the objective evaluation of new medical

or surgical treatments in joint, face or intestinal disorders in animal models (Patsikas et al, 2003), (Patsikas et al., 2004), (Mavrogianni et al., 2004), (Patsikas et al, 2005), (Constantinidis et al., 2005), (Kyrkos el al., 2013).

The contribution of laboratory animals to diagnostic imaging research is of outmost importance. It is, however, very important to stress that this kind of investigations have also led to the refinement of experimental procedures and the reduction of the number of the animals used, as well as the improvement of animal welfare in the field.

Diagnostic imaging techniques are non-invasive in their majority and offer the possibility to define earlier and timely humane endpoints for the animals in the case of detection of irreversible diagnostic findings. Furthermore, they offer the possibility to make repeated measurements in the same animal, which helps the researchers plan earlier interventions and gather data like tumor size in significantly less animals without having to sacrifice them, whilst they may serve as their own control of the following measurements (Brønstad and Dontas, 2011).

On the other hand, there are pitfalls when using animals for diagnostic imaging purposes, which should not be overlooked. Severity classification should take place depending on the impact of anaesthesia used in various techniques (ie. health status of the animal, handling techniques, injection manner of contrast media and anaesthetic risk). It is accepted that many diagnostic imaging techniques require different time slots (from some minutes to several hours) in order to be performed, inducing, different risk levels for the animals under anesthesia, especially if they suffer from e.g. cancer or circulatory failure, where anesthetic protocols should be clearly defined to minimize risk. In advance, deaths under anaesthesia during diagnostic imaging should not be overlooked as well, since it is vital for the researchers to estimate whether they are a result of the procedure or the experimental intervention and present the results in their studies accordingly (Brønstad and Dontas, 2011).

It is, therefore, evident that the use of laboratory animals in diagnostic imaging research significantly improves their welfare since the harm/benefit ratio is reduced (Bateson, 1986). Meanwhile, we should not forget that Research and Development often requires the use of more animals and the dilemma of sacrificing more animals now in order to spare the use of many more in the future always pertains.

Despite the significant impairment of funds for the further advance of research in Greece during the last years, many establishments continue to perform significant work in the field of diagnostic imaging research with promising outcome. For instance research institutes that have already obtained modern equipment, such micro - CT devices or positron emission tomography (PET) devices will hopefully submit really outstanding publications that will enhance diagnostic imaging research with the use of animals.

Concluding remarks

The use of animal models in basic and applied diagnostic imaging research has undoubtedly gained wide acceptance among researchers on an international level. Their appropriate and systematic use in Greece from 1983 to 2014 has led to a considerable benefit for diagnostic imaging.

Both funded research projects and theses or other protocols have been accomplished by scientists with various scientific background in academic institutions and public or private research centers in full compliance with the relevant European Directive 86/609/EC regarding the protection of animals used for scientific purposes. The outcomes of the abovementioned protocols have specifically contributed to the development of new diagnostic imaging techniques for the anatomical study, the diagnosis and treatment both of human and animal diseases.

Furthermore they have promoted the evolution of contrast media and the performance of safety tests with their use. It is consequently deducted that continuous scientific research in the field of diagnostic imaging has benefited in different ways from the use of laboratory animals, whilst the perspectives are extremely positive for the future. The foundation of new research centers in the country, as well as the technical updating of the relevant equipment of the existing ones in order to work more effectively with laboratory animals seems quite promising for this field. Of course, the development of advanced imaging tools by themselves is an important area of research as well, where laboratory animals significantly contribute. Finally, the application of diagnostic imaging techniques has significantly contributed to the refinement of animal protocols by setting noninvasive and more accurate endpoints.

Conflict of interest: None reported.

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