Neuroimaging is being increasingly used in the courts, even though understanding and interpreting neuroimaging methods and results can be very challenging—even without attempting to evaluate their potential applications to forensic questions. The sheer volume of available information, research results, and opinions can seem intimidating to forensic practitioners and to mental health professionals in general.

This ground-breaking book, designed as a reference for forensic psychiatrists, starts with a brief overview of the psychiatric applications of the primary neuroimaging techniques currently in most widespread use, positron emission tomography, single-photon emission computed tomography, and magnetic resonance imaging. Subsequent chapters explore the current and potential uses of neuroimaging in civil and criminal forensic contexts. Diagnostic categories addressed include traumatic brain injury, dementia, psychopathy, paraphilias, psychoses and mood disorders. Legal concepts such as admissibility, relevance, and standards of proof are reviewed as they relate to the possible uses of neuroimaging findings in legal proceedings; prior precedents and court decisions are also reviewed. Novel potential applications of neuroimaging, including detection of deception and identification of memory or recognition, are addressed in dedicated chapters. Ethical questions generated by the rapidly evolving field of forensic neuroimaging are explored in detail in a dedicated chapter.

This book will be of great use to practicing forensic psychiatrists, forensic psychologists and forensic neurologists as they are increasingly likely to find themselves being asked to give professional opinions regarding the impact of neuroimaging findings on medicolegal questions such as competence, criminal responsibility, personal injury and disability. The book will be an invaluable resource for forensic practitioners seeking to understand and navigate this new area.

Praise for ‘Neuroimaging in Forensic Psychiatry’: “This is an interesting and important book, both for the professional audience that is likely to read it and, perhaps more importantly, for another audience that needs to read it. It is an education in how neuroscience may affect the law, as well as a stark warning about the limits of our current discourse in law and neuroscience.” Henry Greely, J.D.
Neuroimaging in Forensic Psychiatry
Neuroimaging in Forensic Psychiatry
From the Clinic to the Courtroom

Edited by

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Foreword

This is an interesting and important book, both for the professional audience that is likely to read it and, perhaps more importantly, for another audience that needs to read it. It is an education in how neuroscience may affect the law, as well as a stark warning about the limits of our current discourse in law and neuroscience.

I have been involved in neuroethics and, more specifically, in law and neuroscience, since its inception – or, at least, its ‘re-imagining’ – in 2002. I was one of the co-directors for the Law and Neuroscience Project, a three-year effort funded generously by the MacArthur Foundation that brought lawyers and judges together with neuroscientists and psychologists, with the more-than-occasional philosopher thrown in for extra flavor. This book has 34 authors; only one was involved in the Project. In fact I only recognize the names of three of the authors from the discussions of law and neuroscience. (Nor do I recognize many of the names for their activity in the International Neuroethics Society, another high-profile effort that looks at, among other things, law and neuroscience.) This is not a negative reflection on the quality of these authors, but it is a negative reflection on the nature of our discourse about law and neuroscience. This book is entitled Neuroimaging in Forensic Psychiatry: From the Clinic to the Courtroom. Its authors are, by and large, forensic psychiatrists or researchers with connections to forensic psychiatry. The Law and Neuroscience Project comprised mainly lawyers, philosophers and neuroscientists. It, and the broader discussions it was part of about law and neuroscience, focused not on the path from the clinic, but from the lab to the courtroom (as well as parts of the legal system that exist outside the courtroom).

The intersections of these worlds have been far too few, and too narrow. As this book convinces me, the broad field of law and neuroscience has much to learn from the forensic psychiatrists, who, after all, are regularly involved in applying brain science in courts. And, I believe, forensic psychiatrists could learn useful things, too, from the broader law and neuroscience community.

The first part of the book provides an introduction to neuroimaging technologies that is comprehensive, but that is also accessible to lawyers and judges – at least, to those who are willing to work just a bit at it. The technologies might have been expanded, both to old standbys, such as CT scans and electroencephalograms (EEGs), as well as to upcoming possibilities, like near infra-red laser spectroscopy. But it covers the main bases – PET, SPECT, MRI and fMRI – quite well.

The second part will also prove particularly useful. It provides readers with useful discussions of some of the most legally relevant diagnoses – traumatic brain injury, dementia, psychopathy, pedophilia, psychosis and affective disorders – as well as strong, critical reviews of the current, and possible future, roles of neuroimaging in confirming (or ruling out) those diagnoses. Forensic psychiatrists may want to focus on the discussions of neuroimaging, but many readers from the law will learn much from the careful discussions of the illnesses themselves.
Part III brings us directly to the courtroom and walks through the possible roles of neuroimaging in the most common reasons for testimony by forensic psychiatrists: competency, insanity, mitigation, diminished capacity, risk assessment and personal injury cases. The most valuable sections lay out just how neuroimaging may, or may not, be useful in such cases.

The fourth part looks at some frontier legal issues for neuroimaging. One chapter takes a hard look at detecting deception; the other at detecting memory. These highlight the reality that one exciting possible use for neuroimaging is to read minds – to look at physical brain states and correlate them to present mental states. This cannot reveal what, for example, a defendant was thinking at the time of the alleged offense; the so-called ‘time machine’ problem prevents that. But it may be able to tell us something about their mental states at the time of their subsequent statements. Normally, if we want to ascertain someone’s mental state, the best way to do so is to ask them. But if we cannot trust them to answer honestly, reading their minds may be a good alternative. I only wish this part had roamed a little more broadly across the landscape of possible uses of mind-reading in the law, from detecting whether someone is feeling pain (an enormous issue for the legal system) to determining whether someone is ‘truly’ feeling bias or remorse or guilt.

The last part looks at legal issues in the United States and in England and Wales, and at ethical issues more broadly. This is territory that has been broadly explored in the existing law and neuroscience literature (see, for example, [1–6]); these chapters are clear discussions, and quite useful for forensic psychiatrists, though lawyers, judges and philosophers may prefer more specialized treatments.

Forensic psychiatry and the broader law and neuroscience community need to talk more. The depth and breadth of forensic psychiatry’s knowledge of the technologies, the diseases and the courtroom settings will be of great value to the broader law and neuroscience community. On the other hand, forensic psychiatrists should find value in the deeper discussion of the thorny legal questions – and of the ethical and philosophical questions that lie behind them – that the broader law and neuroscience literature provides, along with the, admittedly speculative, look farther beyond today’s courtroom uses, to future uses – and to the ways technological change and social change may intertwine to produce surprising results. It is unfortunate, and somewhat surprising, that these perspectives have not yet been better integrated. One can say the field is young or, at least, newly reconceptualized, but the current neuroethics field is approaching the end of its first decade. We should not let this distance continue into its second.

Which leads to my last point. Bringing all the relevant expertise and perspectives together into this field is not just ‘good’ but important, because the field is important. Neuroscience is vastly increasing our ability to predict, understand and modify the workings of the human brain. The law is about human brains, and only incidentally about the flesh in which they are embodied. Knowing more about future behaviors, or about present mental states or about how to change mental states or behaviors will necessarily be of great interest to the law (and to the rest of society). But knowing more about the science of the human brain is not the same as knowing enough about how to use that new knowledge. Wayne Drevets, Jonathan Savitz and Joseph Simpson end their chapter on affective disorders with some carefully hedged prophecy, with comments specifically about affective disorders but applicable much more broadly to law and neuroscience:

Looking forward, it seems reasonable to anticipate that as the evidence base continues to accumulate, neuroimaging may be used increasingly in legal cases to buttress
FOREWORD

a diagnosis of mood disorder. It is conceivable that in the future the development of valid and reliable diagnostic neuroimaging biomarkers will serve to diminish the common perception among the general public, and even among many attorneys and judges, that mood disorders (among other common psychiatric diagnoses such as PTSD and other anxiety disorders, etc.) are purely ‘psychological’ conditions, devoid of a detectable physical basis. Ultimately, the availability of such clinical diagnostics may lead to significant changes both in the nosology of psychiatric disorders and in the definitions applied in legal areas such as disability, workers’ compensation, tort liability and others. However, it is also undoubtedly true that, just as with any other proposed scientific evidence, attempts to use imaging data to draw conclusions that are more broad than the results can actually support will not pass muster in the courts.

Neuroimaging not only may be used in courts, it is already being used and its possible applications are increasing. It not only may change public perceptions about mental conditions, it already is. It has not yet led to changes in the definitions of diseases (and of ‘normal’ variations) used in medicine and law, but it will. But our biggest fear should not be that efforts to introduce into courtrooms unjustified conclusions from neuroscience will not pass muster, but that they will pass muster – or not be put to the test at all. The potential downside is not that litigants overreach, unsuccessfully, wasting the system’s time and money, but that they overreach successfully, putting lives, justice, liberty and truth at risk. I cannot now answer the question of which technologies will prove appropriate for which uses – no one can, yet. But I am certain that we, as a society, along with other societies around the world, will be forced to answer that question. To do so well we will need all the mental resources – all the brains – we can muster. All of us worrying about these questions must work together if we are to have a chance even to muddle through, avoiding catastrophic mistakes.

Joseph Simpson, this book’s editor, states in the book’s introduction that ‘The intended audience is practicing forensic psychiatrists and psychologists,’ but then goes on to predict that ‘psychiatrists and psychologists who are not currently involved in forensic work, as well as neurologists, radiologists, attorneys and judges will be able to use this book.’ Niels Bohr, the Danish nuclear physicist, is often credited with having said ‘It’s always hard to predict things, especially the future.’ Actually, it is easy to make predictions; it is just hard to be right about them. I hope Simpson’s prediction is right – it certainly deserves to be.

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FOREWORD

Introduction

The past several decades have witnessed a tremendous expansion in the technological ability to visualize the structure and functioning of the living human brain. Imaging methods such as magnetic resonance imaging (MRI), positron emission tomography (PET) and single-photon emission computed tomography (SPECT) are now routinely used in the evaluation of neurological diseases and conditions such as cancer, multiple sclerosis, stroke and traumatic brain injury. The years ahead promise further improvements in these and other imaging techniques.

Tools in the researcher or clinician’s armamentarium for examining the structure and function of the human brain in vivo are often referred to as neuroimaging modalities. For consistency and simplicity, this term is used throughout this book to describe techniques which are used to produce images of the structure, activity or distribution of biological molecules within the living brain. In the field of psychiatry, the primary clinical application of neuroimaging at present is to rule out neurological or ‘organic’ causes of psychiatric symptoms. While there is a large and constantly expanding body of research applying neuroimaging techniques to mental disorders, neuroimaging has not yet entered the mainstream of routine clinical practice in psychiatry.

This is likely to change in the near future. Many researchers predict that neuroimaging will soon be used to more accurately diagnose psychiatric conditions, as well as to predict and monitor patients’ responses to medications or other treatments. As accuracy, reproducibility and standardization increase, and as the cost of performing the tests falls, neuroimaging techniques will be added to the toolbox of clinicians treating patients. It is unlikely that psychiatric neuroimaging will remain the sole province of research scientists for much longer.

As neuroimaging enters clinical practice, so too will it find its way more and more into legal proceedings. The legal arena has seen imaging results offered as evidence for a psychiatric diagnosis as far back as three decades ago, when a computerized tomography (CT) scan was introduced to support a diagnosis of schizophrenia at the insanity trial of John Hinckley, who shot President Ronald Reagan and three others in 1981. This foreshadowed the burgeoning use of all manner of imaging data in court. In the 1990s and 2000s, data from MRI, PET and SPECT scans have been introduced in hundreds, if not thousands, of civil and criminal proceedings in the United States and many other countries. In some cases, the proffered evidence was ruled inadmissible, but in many other cases judges have allowed imaging data to be presented at trial. Of course, the impact of such evidence on the final decision by the trier-of-fact (i.e., judge or jury) is a critical question – the fact that evidence is allowed to be heard does not necessarily mean that it will be persuasive, or even that it will be considered at all.

The field of forensic psychiatry is approaching a crossroads. As neuroimaging becomes ever more reliable, standardized and informative, attempts to use its results in civil and
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criminal proceedings of all types will increase dramatically. Accurate diagnostic tests for mood disorders and anxiety disorders such as post-traumatic stress disorder (PTSD) could potentially revolutionize the field of mental health disability litigation. In criminal justice, some observers anticipate profound changes in how the legal system assesses and manages criminal defendants with psychiatric conditions, or even criminal offenders in general. Others disagree, and predict that the role of neuroimaging in the criminal justice system will remain peripheral.

The unprecedented ability of sophisticated techniques such as functional MRI (fMRI) to create images of an individual’s neural responses to a single stimulus event has created the possibility of entirely novel applications, such as the detection of deception and the identification of memories. Already the use of fMRI for lie detection has moved out of the realm of science fiction, but the technique has by no means become widely accepted. Some question whether it will ever be specific and reliable enough for any applications outside of cognitive neuroscience research.

In an intriguing 2008 study, researchers were able to categorize whether their subjects were thinking about tools or about dwellings by analyzing their fMRI data [1]. This finding suggests the possibility of a primitive form of ‘mind reading,’ and garnered attention in the popular media [2]. Clearly, the potential implications of such a capability are profound.

The idea of using neuroimaging for legal purposes has its share of skeptics. The statistical nature of functional neuroimaging studies and the wide variability among individual brains have been suggested as fatal flaws for those who hope to introduce what amount to probabilities into a context that demands categorical answers. More fundamentally, a number of authors have questioned whether neuroimaging results can be meaningfully applied to essential legal questions such as intent, state of mind and causation. Some have directly accused the advocates of so-called ‘neurolaw’ of intending to use neuroimaging as a lever to completely redefine the criminal justice system, such that free will and personal responsibility disappear, replaced by deterministic chains of causation beyond the control of the individual criminal defendant [3, 4].

Even if the technological and methodological obstacles to using neuroimaging in the courtroom can be overcome, a number of legal and ethical questions arise. To cite only a few from the criminal context, how would performing a neuroimaging study on a criminal defendant impact that person’s rights, such as the right to be free of unreasonable search and seizure, or the right against self-incrimination? The potential risks of rushing to adopt new technologies before they have sufficiently matured have also been pointed out [5].

The purpose of this book is to provide a frame of reference in which to consider the current and potential future applications of neuroimaging in forensic mental health. It will examine in detail the limitations of using neuroimaging in court, as well as the unanswered questions that arise as the field of neuroimaging evolves, and attorneys and mental health professionals seek to apply its findings in legal proceedings. The intended audience is practicing forensic psychiatrists and psychologists. Forensic practitioners are increasingly being asked to respond to or interpret neuroimaging findings as they are applied to core medicolegal questions such as competence, criminal responsibility, personal injury, disability, and so on. The book is designed as a resource to help forensic practitioners understand and navigate this new area, and to gain an appreciation of topics of disagreement and controversy within it.

In addition, psychiatrists and psychologists who are not currently involved in forensic work, as well as neurologists, radiologists, attorneys and judges will be able to use this book to further their knowledge of the growing subject of neuroimaging in forensic
psychiatry. The overarching objective is to give the reader a practical, realistic idea of what neuroimaging is likely to contribute to the field of forensic psychiatry – as well as which techniques, applications or results are unlikely to be useful in the courtroom.

This endeavor first requires an overview of the scientific underpinnings and methodological implementations of neuroimaging techniques. Part I provides this essential background information. Part II reviews the current state of neuroimaging as it pertains to a number of the psychiatric conditions most often relevant in the civil and criminal legal arenas.

Once this groundwork is laid, the myriad and often thorny issues inherent in attempting to present neuroimaging evidence in the legal context will be discussed. Part III examines the possible applications of (relatively speaking) ‘traditional’ neuroimaging techniques, i.e., those aimed at clarifying a psychiatric diagnosis, to legal questions in the criminal and civil courts.

In Part IV, we go beyond psychiatric diagnosis to review some of the latest proposed uses of neuroimaging: ‘lie detection’ and the use of neuroimaging to identify memories and assist in interrogations.

Part V concludes our survey of neuroimaging in the courtroom by examining in detail the practical legal obstacles to its widespread adoption, and discussing the broader legal and ethical concerns raised by these scientific advances. As the techniques evolve, society will be confronted with questions about whether to allow certain types of information to be obtained, under what circumstances and with what safeguards.

There is no doubt that neuroimaging holds great potential for the mental health field, in both the research and clinical domains. In clinical psychiatry, this potential is only beginning to be realized. It is the aim of this book to demonstrate that neuroimaging also holds significant potential value in the legal domain. However, there are many practical as well as ethical questions which the legal system, and by extension society as a whole, must deal with in order to guard against misuse and to foster the proper use of these revolutionary techniques.

Joseph R. Simpson

References

Part I

Imaging Techniques
1 PET and SPECT

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Introduction

Nuclear medicine is a medical imaging subspecialty that uses administered radioactive materials to create images that assist in the diagnosis and treatment of disease. Positron emission tomography (PET) and single photon emission computed tomography (SPECT or SPET) are tomographic nuclear medicine techniques commonly used to diagnose malignant, inflammatory, degenerative and circulatory disorders.

Tomography is an imaging approach that involves reconstruction of a dataset into three-dimensional (3D) images. It allows higher contrast and improved visualization of structures that would obscure each other on planar images, such as superimposed lung, heart and thoracic spine on a conventional chest X-ray. Tomography first came into widespread use using X-rays in computed tomography (CT). The principle of tomography is now used in most 3D medical imaging techniques.

Both PET and SPECT use cameras to detect photons emitted by the radioactive decay of unstable isotopes, which can be radioactive elements themselves, radioactive isotopes synthesized into molecules of interest or radioactive isotopes attached to molecules, to create functional images. These radioactive materials are called radiotracers because they are able to trace processes of interest without perturbing the processes being followed. PET and SPECT differ in the type of isotopes they require, the way they detect the emitted signals and the way the data are reconstructed into images. SPECT is technically simpler, less expensive and has lower spatial and temporal resolution than PET. A forensic practitioner can encounter PET and SPECT scans introduced as evidence of abnormal brain function at various stages of legal proceedings.

A chemical element is defined by two parameters: atomic number and atomic mass. Atomic number is the number of protons present in an element and determines the chemical properties of that element. The number of protons and electrons in a given element are fixed. Atomic mass is the total mass of protons, neutrons and electrons in a single atom of a given element. The atomic mass can change based on the number of neutrons.

Atomic mass and atomic number are denoted in superscript and subscript, respectively before the capital letter that signifies the element. For example, $^{18}_9$F is an isotope of fluorine with an atomic mass of 18 and an atomic number of 9. Atomic mass can also be listed after the symbol of an element. For example, $^{18}$F can also be denoted F-18 or Fluorine-18.
Isotopes are atoms of the same chemical element that differ in the number of neutrons contained in their nuclei, which changes their atomic mass. The nucleus of the atom is made up of protons, which have positive charge, and neutrons, which have no charge. Because the positively charged protons repel each other, it takes a great deal of energy to hold the nucleus together. Further, it requires a delicate balance between the number of neutrons and the number of protons in a nucleus for that nucleus to remain intact. If a nucleus has too many or too few neutrons to remain intact, it is called unstable or radioactive.

Radioisotopes are unstable isotopes of chemical elements that become more energetically stable through the release of energy or particles (called radioactive decay). This radiation can be released in multiple forms including: $\alpha$-particles, which are equivalent to He$^{2+}$ helium nuclei and include two protons and two neutrons; $\beta^-$ particles, which are electrons and allow a proton to convert to a neutron; $\beta^+$ particles, also called positrons, which are exactly the same physically as $\beta^-$ particles except they have a positive charge (and form the basis for PET imaging); and $\gamma$-rays, which are high-energy photons physically the same as X-rays except that they originate from the nucleus whereas X-rays originate from the electron shell, and the range of $\gamma$-ray energies goes higher than that for X-rays, as shown in Figure 1.1 [1] \(\alpha\) and $\beta^-$ particles typically travel a distance of microns to millimeters in tissue, making them difficult to detect externally, whereas $\gamma$-rays travel at the speed of light and are very likely to exit the tissue where they can be detected. Positrons ($\beta^+$ particles) have a very interesting fate: when a positron is ejected from the nucleus it briefly combines with an electron to form a quasi-atom called a positronium. However, this construct is unstable and lasts a tiny fraction of a second. The positron and electron then annihilate (that is, they both cease to exist) and their energy is released in the form of light. Specifically, the annihilation results in exactly two photons with 511 keV of energy moving in opposite directions. While there is a wide range of possible mechanisms for radioactive decay, each specific isotope has a characteristic mode or modes of decay.

Radioactive decay is an exponential process, meaning that for a given isotope there is a characteristic period of time during which one half of the atoms will undergo decay. This
is known as the half-life \( (t_{1/2}) \). Half-lives of known isotopes can range from fractions of a second to thousands of years, but almost all medically useful isotopes have half-lives in the range of minutes to days, with the most commonly used having half-lives from about 2 to 6 hours. For example, the half-life of \(^{14}\text{C} \), which is used in carbon dating, is 5730 years, which makes it excellent for estimating the age of prehistoric specimens but undesirable for most types of clinical imaging, whereas \(^{18}\text{F} \) has a half-life of 110 minutes and decays by positron emission, making it ideal for PET imaging. In addition to the half-life of the isotope itself, called the physical half-life, when the isotope is given to a patient in some chemical form, that molecule may also be excreted from the body at some rate, called the biologic half-life. The effective half-life is the rate at which the radioactivity disappears from the body and is a combination of the physical decay and the excretion. For example, a radioactive molecule that has little or no excretion from the body will have an effective half-life very similar to the physical half-life, whereas a radioactive molecule that is very quickly excreted will have a very short effective half-life even if the physical half-life is very long. Because it is a combination of physical and biologic clearance from the body, the effective half-life is never more than the shorter of the physical or biologic half-life.

**PET radiochemistry**

Radioisotopes used in clinical PET are energetically unstable forms (isotopes) of the main elements found in the body – carbon (C), oxygen (O) and nitrogen (N). The natural concentrations of those isotopes are extremely low, so they must be artificially generated in a cyclotron. In nuclear medicine, radioligands are molecules that carry the radioactive isotopes to their targets in the body. The process of inserting a radioactive isotope into a biologically active molecule is called radiolabeling.

Simple molecules normally used by the body, such as glucose, water or ammonia, as well as more complex molecules such as a substrate for the dopamine transporter [1, 2], can be used as radioligands. An isotope combined with a ligand is called a radiotracer or a radiopharmaceutical, which is administered to the patient.

Fluorine-18 (\(^{18}\text{F} \)) is the isotope most commonly used in clinical PET due to its many advantageous properties [3]. The \( t_{1/2} \) of \(^{18}\text{F} \) is 110 minutes, which is long enough to transport it over relatively long distances from the production site, but brief enough to limit radiation exposure from isotope remaining in the body after the scan. Moreover, radiolabeling glucose with \(^{18}\text{F} \) by substituting the hydroxyl group in a regular glucose molecule to create the radioligand 2-deoxy-2-(\(^{18}\text{F} \))-fluoro-D-glucose (\(^{18}\text{FDG} \)) is a reliable and well-established process accessible to most qualified radiochemists. \(^{18}\text{FDG} \) is a glucose analog that is taken up by brain cells like regular glucose, but it neither undergoes oxidative metabolism (glycolysis) nor is it released back into the circulation.

Other elements used in brain PET are significantly more difficult to use. For example, \(^{15}\text{O} \) has a half-life of just over two minutes, making on-site production essential for \(^{15}\text{O} \) (\( \text{H}_2\text{O} \)) PET. Moreover, since \(^{15}\text{O} \) is used to label water, it provides information on regional brain blood flow, which is similar to what can be obtained by certain types of SPECT and MRI scans at much lower cost and technical complexity. While O-15 H_2O PET studies were critical in the early days of brain-imaging research, and data obtained with it may still be encountered in court, it is difficult to justify its clinical use today. Likewise, \(^{13}\text{N} \) and \(^{11}\text{C} \) have short half-lives of 10 and 20 minutes respectively and have higher energy.
Table 1.1 Half-lives and energy of the main isotopes used in PET

<table>
<thead>
<tr>
<th>Isotope</th>
<th>$t_{1/2}$ (minutes)</th>
<th>Energy (kiloelectron volts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}$C</td>
<td>20.4</td>
<td>960</td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>2.07</td>
<td>1190</td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>109.7</td>
<td>640</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>9.96</td>
<td>1720</td>
</tr>
</tbody>
</table>

Ionizing radiation deposits energy into tissues that is measured in joules/kg, a unit also known as a sievert (Sv). Table 1.1 lists the half-life and energy of the main isotopes used in PET.

**SPECT radiochemistry**

SPECT radioligands come in two general categories: brain blood flow tracers and molecular probes of brain receptors and neurotransmitters. The latter category is not yet commonly seen in forensic practice. Effective half-life of the radioligand is determined by the half-life of the radiotracer used to label it and the elimination rate of the biologically active compound that carries it.

Compounds used for SPECT are typically low-molecular weight and lipophilic, allowing them to easily cross the blood–brain barrier [4]. The blood flow (perfusion) tracers are distributed in the brain in accordance with regional blood flow over a known period of time, usually measured in minutes, providing an average image of brain perfusion over a fixed time period of a few minutes. SPECT image acquisition is timed to begin at the end of the estimated ‘distribution time’ of the radioligand.

The gamma ray-emitting radioligand most commonly used in brain SPECT is technetium-99m ($^{99m}$Tc) [5]. $^{99m}$Tc is produced from molybdenum-99 ($^{99}$Mo), which itself has a half-life of 66 hours, making it easy to generate. $^{99m}$Tc derived from $^{99}$Mo is delivered on a weekly basis to most clinical nuclear medicine departments. $^{123}$Iodine ($^{123}$I) is a SPECT radioisotope that used to be popular in perfusion SPECT [6]. While $^{99m}$Tc has a half-life of six hours and emits a photon that has energy of 140 keV, $^{123}$I has a distribution time of about one hour, half-life of 13 hours and a 159 keV photon. These characteristics make I-123 inferior to Tc-99 in brain perfusion SPECT [3].

**Radiation exposure**

Because the energy released by radioactive decay can cause ionization of molecules in living tissues, it is called *ionizing radiation*. The gray (Gy) is the SI unit of absorbed radiation dose, defined as the deposition of one joule of energy in one kilogram of tissue. The ionizations from radiation deposition can cause a range of effects, which are termed biological toxicity. Toxic effects may include: single-stranded DNA breaks, which can be repaired; double-stranded DNA breaks, which are lethal to the cell; and DNA base mutations, which can be carcinogenic. Biological toxicity varies both with the type of radiation and with the organ being exposed to the radiation. For example, the bone marrow and gonads are much more sensitive to the effects of ionizing radiation than brain tissue. Further, $\alpha$-particles are far more likely to cause cell death than $\gamma$-rays. In order to be able
to compare radiation doses from different sources to different organs, a weighted quantity called the effective dose is used. The effective dose is expressed in SI units as sieverts (Sv) but in the US is still frequently reported in units of roentgen equivalent man (rem) or in millirem (mrem), which is one thousandth of a rem [7].

Rem and millirem can be converted in a straightforward way to the SI unit, sievert:

\[
1 \text{ rem} = 0.01 \text{ Sv} = 10 \text{ mSv} = 10000 \mu\text{Sv}
\]

\[
1 \text{ millirem} = 0.00001 \text{ Sv} = 0.01 \text{ mSv} = 100 \mu\text{Sv}
\]

Ionizing radiation is present in space and is attenuated, but not completely eliminated, by Earth’s atmosphere. In addition, naturally radioactive isotopes are present in different concentrations in our environment. For example, Radon (Rn) has 36 radioactive isotopes with atomic masses ranging from 193 to 228 and is a common source of naturally occurring exposure to ionizing radiation. Thus, we are constantly exposed to low levels of radioactivity.

The average person in the U.S. receives an effective dose of about 3.6 mSv of radiation per year from naturally occurring materials and cosmic radiation. Due to reduced atmospheric protection, people are exposed to an additional 5 μSv of cosmic radiation per hour on an airplane flight at the common altitudes of 30 000 feet and higher.

In the U.S., the Occupational Safety and Health Administration (OSHA) limits workplace exposure to 50 mSv per year for non-pregnant adults with occupations involving radioactive materials. For minors working in or near radioactive materials, the limit is 5 mSv per year. For people of any age not working in occupations involving radiation, the limit is 1 mSv per year. The National Council on Radiation Protection and Measurements (NCRP) sets guidelines for pregnant workers [8]. The radiation dose to the embryo/fetus resulting from occupational radiation exposure to the mother should not exceed 5 mSv from the time when the pregnancy is declared to the radiation safety monitoring staff at the place of work until delivery. Women who may become pregnant should limit their occupational radiation dose to no more than 2.5 mSv per month, so if a pregnancy is confirmed, the total radiation dose received by the embryo/fetus during the first two months would not exceed the 5 mSv fetal dose limit. The council advises that pregnant workers should avoid or reduce radiation exposure in the workplace [8].

Doses of radiation below 1 Sv are unlikely to produce any immediate detectable changes in humans, though they have risk of inducing mutations which may lead or predispose to cancer formation at a later time. 1–2 Sv will cause illness but will rarely be fatal. Acute full body exposure of 5 Sv will kill 50% of people exposed, and doses that exceed 10 Sv are always fatal.

A PET scan of the brain with $^{15}$O water exposes the subject to 1 mSv of radiation. In comparison, a SPECT scan with $^{99m}$Tc HMPAO delivers 6.9 mSv of radiation. A whole body $^{18}$FDG PET is associated with 7–14 mSv of radiation, depending on dose and technique. Thus, radiation exposure from any single nuclear medicine scan is far below levels associated with known harm and should not present a risk of any immediate radiation-induced illness. A single nuclear medicine scan is significantly below the annual limits for persons with occupational exposure to radiation, but clearly above the recommended limits for people not working with or near radioactive materials. There is also a lifetime limit. With an increasing number of scans in a single patient, an increase in cancer risk can be expected and should be included in risk/benefit ratio considerations. While the risk
of cancer induction from ionizing radiation from diagnostic imaging studies is real (and unnecessary exposures should be avoided), it is impossible to accurately estimate the risk from a given scan, though the risk is certainly very low. Therefore, diagnostic radiation exposures should be avoided if unnecessary, but useful studies should not be withheld due to giving too much weight to the risks of the radiation exposure.

A number of routine clinical procedures can be employed to minimize the patient radiation dose from PET or SPECT studies. Patients are requested to empty their bladder prior to injection with the tracer and again after the study to minimize radiation exposure to the urinary bladder, which is the organ that receives the largest radiation dose from many agents used.

While it is not possible to estimate an individual’s risk of cancer related to a single PET or SPECT scan, the population-based increase in cancer risk has been estimated for the use of CT scanners. A recent study estimated that CT scanner use in the U.S. would expose patients to enough ionizing radiation to induce 1.5% to 2% of future cancers [9]. A second study estimated that development of cancer from CT scan exposure will vary widely depending on the specific type of CT examination and the patient’s age and sex. According to this study, an estimated 1 in 270 women who underwent CT coronary angiography at age 40 years will develop cancer from that CT scan (1 in 600 men), compared with an estimated 1 in 8100 women who had a routine head CT scan at the same age (1 in 11 080 men). For 20-year-old patients, the risks were approximately doubled, and for 60-year-old patients, they were approximately 50% lower [10]. However, these estimates derive from mathematical models and have not been verified with empiric evidence. Furthermore, the lifetime risk of developing malignancy is so high (on the order of 1 in 2), that detecting an additional 1 in 270 risk above that high level would require an impossibly large sample size.

Currently, it is unknown whether increased use of nuclear medicine studies will one day be associated with actual increases in population-based cancer risk. To avoid unnecessarily increasing cancer incidence in future years, every clinician must carefully assess the expected benefits of each PET and SPECT scan ordered for forensic purposes and fully inform forensic evaluatees of the known risks of radiation.

**Physics of PET and SPECT signals**

For both PET and SPECT scans, the radioactive tracer is almost always injected into a peripheral vein after placement of an intravenous line. Therefore, patients must be able to tolerate an intravenous line access. Once injected, the tracer distributes in the body based on its uptake, delivery, metabolism and excretion properties. In some cases, imaging is done during the distribution time to evaluate the kinetics of distribution, but in most cases, the patient waits in a basal state, sitting or lying quietly in a dimly lit room, during distribution and is imaged once the patient is at or near steady state. Distribution time varies based on the tracer. Some tracers take hours to distribute, whereas others distribute within minutes. After injection of a SPECT tracer a patient may wait in a waiting room or may leave and return to the clinic in time for the scheduled scan. In contrast, patients awaiting PET are typically isolated after injection to minimize radiation exposure to staff and the public as photons emitted after positron decay are much higher than those from $^{99m}$Tc SPECT tracer decay: 511 keV versus 140 keV respectively. After the tracer has distributed, the patient is positioned in the scanner.
Though both PET and SPECT utilize photons emitted during nuclear decay for image formation, they differ in the source and nature of these photons. In SPECT, a single photon is emitted in the decay of $^{99m}$Tc and detected by two or three gamma cameras rotating around the patient [11]. With PET, the process is more complicated. PET isotopes undergo radioactive decay via a process known as positron emission or positive beta decay. During this decay a positron and a neutrino are emitted from the radiotracer. The emitted positron travels through the tissue, until it collides with a random electron and both are annihilated (Figure 1.2). The distance the positron travels before annihilation depends on the positron energy (Table 1.1); the lower the energy, the less distance traveled. For $^{18}$F, the positron range is less than 2 mm. The higher the positron energy, the farther the positron will travel before annihilation, and therefore the more uncertainty there is in where the positron actually originated, ultimately leading to lower spatial resolution. Therefore, lower energy positron emitters provide higher resolution imaging. During annihilation, two gamma-rays with energy of 511 keV are released in opposite directions at a $180^\circ$ angle from each other and are detected by the PET scanner cameras that are arranged in a stationary ring around the patient. Below we will review separately how SPECT and PET scans capture, count the photons and turn data into images yielding important information about brain function.

**SPECT image generation**

The simplest form of photon tomography is rotational SPECT. This approach uses a single gamma camera rotating around a stationary patient in a circular or elliptical orbit. Most modern SPECT scanners are equipped with two or three cameras, reducing the time of acquisition and the distance each camera must travel around the patient for each image [12].

The rotation of the SPECT camera head subjects the SPECT system to forces not encountered in other tomographic systems. Thermal, magnetic and gravitational forces must be accounted for in the SPECT scan design.
Data acquisition for SPECT

Unlike in PET scans, the tracer used in SPECT emits gamma radiation that is measured directly by a scintillation counter also known as a gamma camera. The camera is made up of a collimator, a crystal and an array of photomultiplier tubes. The collimator, in most cases, is a block of lead with an array of parallel holes. These holes are perpendicular to the crystal and they allow only the photons that are perpendicular to the crystal to pass. The collimator design ensures that the scintillation camera records only the photons that come directly from the patient. However, a limitation of this design is that only a limited number of photons are actually detected, increasing the image noise and the image formation time [13]. The crystal is a material that emits flashes of visible light known as scintillations when high-energy X-ray or γ-ray photons strike it. The most commonly used gamma camera crystals today are sodium iodide crystals doped with thallium [14]. The light emitted by the scintillator hits the surface of the nearest photomultiplier tube. The photomultiplier tube converts a flash of light into an electrical signal that allows measurement of the energy of the incoming γ-ray. The array of photomultiplier tubes utilizes a method called Anger logic to accurately localize the point where the incident γ photon struck the crystal.

A series of images are produced as the cameras move around the patient and record data from multiple angles. Most SPECT scans use a ‘stop and shoot’ technique in which the camera briefly pauses at multiple steps in the orbit to allow for data recording. A 360-degree arc is usually needed to acquire an adequate image. The camera typically pauses to shoot an image every 3–6 degrees. The more angles obtained by the camera, the better the resolution of the image.

SPECT spatial resolution is approximately one centimeter using typical clinical instrumentation. The total scan time is typically around 20 minutes. Patient motion and the amount and specific activity of the radiopharmaceutical affect image quality [14]. Whereas longer imaging times give more data, reducing image noise, the longer the scan the more likely the patient is to move, which degrades the image significantly. While immobilization devices can be used to attempt to minimize patient motion, they are of limited effectiveness. Most patients cannot reliably keep their head still for longer than 20–30 minutes, so imaging times longer than this are usually counterproductive. In some patients, particularly those with neurologic or psychiatric disorders, even 20–30 minutes is difficult to achieve without motion. Periodic coaching and encouragement by the imaging team can help prevent patient motion.

Image reconstruction

In SPECT a number of corrections must be made for background and physical effects. First, the projection images need to be corrected for non-uniformity and axis-of-rotation misalignment. Once these corrections, which are beyond the scope of this chapter, are applied, the multiple projection images are reconstructed to form a three-dimensional image. The simplest reconstruction technique is filtered backprojection, which, for example, is routinely used to create X-ray computed tomography (CT) images. However, for images which have relatively low counts, filtered backprojection results in three-dimensional images that have many ‘streaky’ artifacts. Another approach, called iterative reconstruction, starts with a filtered backprojection image then uses mathematical models to essentially guess at a better solution. Doing multiple iterations of the algorithm arrives at a closer solution to how the image should appear. While iterative reconstruction is computationally demanding, modern computers permit its use and the gains from iterative reconstruction