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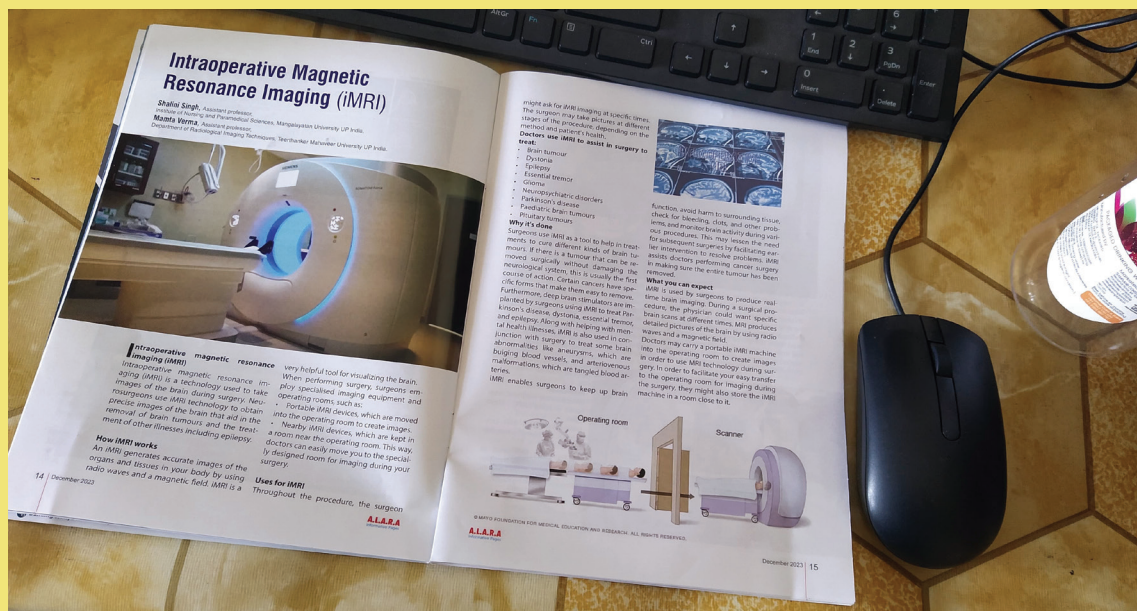
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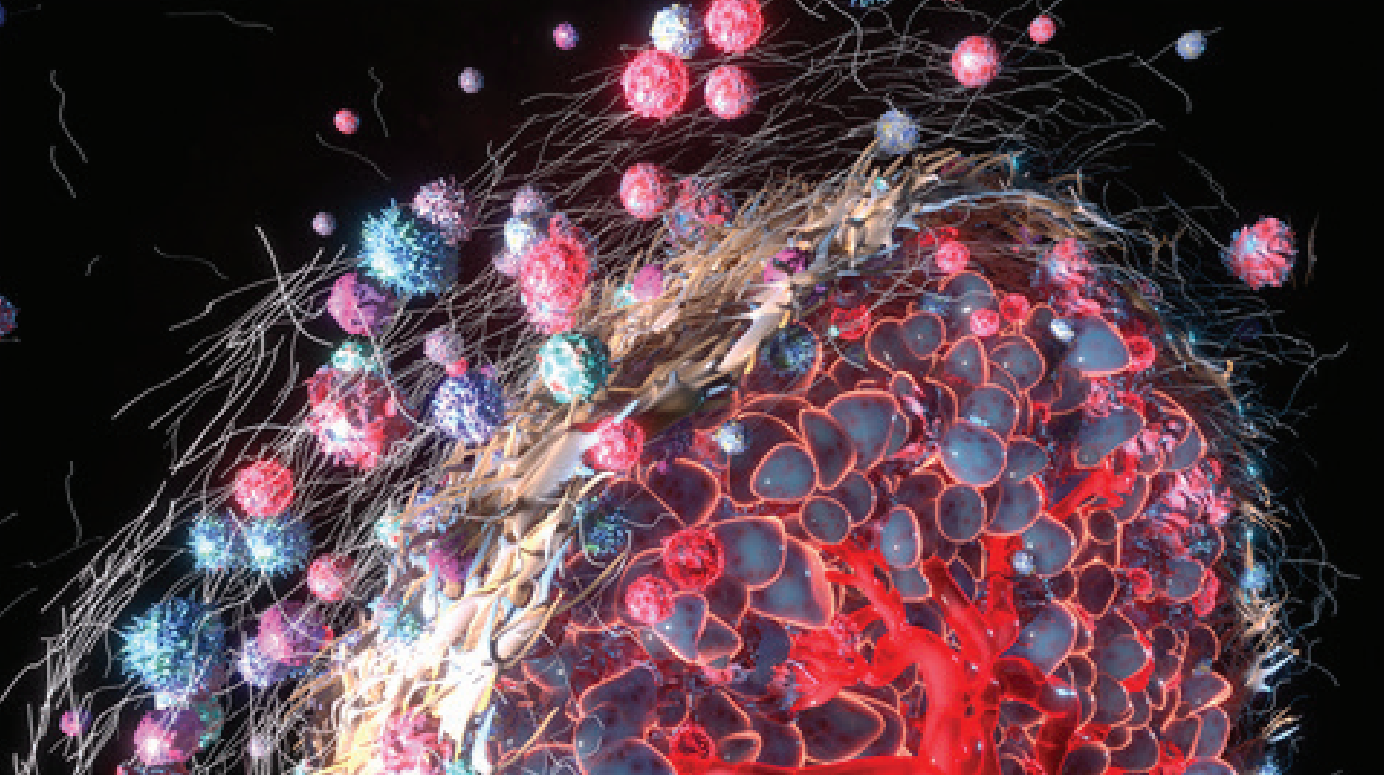
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# Progress in the manufacturing of RADIOTRACERS

**Shipra Saroj**, Research fellow; **Mamta Verma**, Assistant Professor  
**Sohel Rana**, Research fellow; **Sajjad Ali**, Research fellow  
**Pratyeksha**, Research fellow

Department of Radiology Imaging and Techniques,  
College of Paramedical Sciences, Teerthanker Mahaveer University, Moradabad, UP

In contemporary healthcare, nuclear medicine is becoming more and more important as a diagnostic tool. Position emission tomography (PET) in particular has made significant advancements since it has better imaging capabilities than single photon emission tomography (SPECT). The most notable is the roughly two orders of magnitude higher sensitivity of PET, which is determined by the probability of finding a nuclear decay occurring within a patient's body. The fact that contemporary whole-body PET scanners may achieve 4-5 mm of spatial resolution while SPECT systems usually have far lower resolutions in the 8-10 mm range is also significant. Additionally, photon attenuation correction for PET is simpler and more accurate, producing pictures that most accurately depict the absolute radiotracer concentration in-vivo.

PET became a cutting-edge biomedical research instrument in the middle of the 1970s, available only to the world's largest research institutions. The development of the combined PET/CT scanner which has dominated the PET scanner market since 2001 and significantly increased the availability of clinical PET, was a primary driving force behind the major clinical breakthrough for PET. The



technically more ambitious PET and/or MR scanner and various imaging systems for pre-clinical research are also part of the modern PET imaging instrumentation. The creation of potent tracers, which again rely on the availability of radionuclides with appealing chemical and physical features like half-life and emissions during decay, has played a significant role in the more recent success of PET. The fact that light elements like carbon, nitrogen, oxygen, and fluorine are among the most commonly used radionuclides is especially noteworthy because it makes it easier to label compounds that are chemically identical to endogenous substances—a tactic that is not feasible with the classical radionuclides used for SPECT.

The most significant scientific and technological advancements that have an impact on the creation of PET radiotracers will be discussed in this review article. The review will begin with a brief historical overview before concentrating on the most recent developments and the state of PET tracer production at the moment. Lastly, a number of potential novel developments in the future will be examined.

### **An overview of the past**

Particle accelerators were created and made Lawrence as a tool in physics labs about a century ago. Leo Szilard created and patented the linear accelerator in 1928. Ernest O. Lawrence<sup>6</sup> created the cyclotron in Berkeley, California between 1929 and 1930. The cyclotron was patented in 1932. Even though it was highly developed and mostly utilized for radiation physics, the research programme was more focused on producing radionuclides after Irene and Frederic Joliot-1934 Curie's discovery of artificial radioactivity. Not long after cyclotron-produced radionuclides became available, George de Hevesy and others used <sup>32</sup>P to investigate phosphorus metabolism in rats. Additionally, Sam Ruben and Martin D. Kamen studied plant physi-

ology with [<sup>11</sup>C] CO<sub>2</sub>. Nevertheless, they quickly shifted to the recently discovered <sup>14</sup>C after recognizing that the 20.4-minute half-life of carbon-11 is a limiting issue in their research. Following the 1938 discovery of nuclear fission by Hahn and Strassmann and the 1942 demonstration of the first self-sustaining nuclear chain reaction by Fermi and associates, the availability of radionuclides produced by reactors, such as <sup>3</sup>H, <sup>14</sup>C, <sup>35</sup>S, <sup>32</sup>P, and <sup>125</sup>I, increased quickly. These radionuclides are now widely used in almost every branch of science. The field of nuclear medicine was primarily founded in 1941 when Saul Hertz and Arthur Roberts used <sup>130</sup>I/<sup>131</sup>I, the first radionuclide produced by a cyclotron, to treat hyperthyroidism. Before the first practical scanners were produced in the middle of the 1970s as a result of advancements in positron emission tomography technology, the use of positron emitters in many scientific fields was largely ignored.

Despite the fact that the fundamentals of cyclotron technology have not changed since the early 1930s, significant advancements in the RF system and target technology, for instance, have led to the development of extremely potent medical cyclotrons. Medical cyclotrons are characterized by proton only or proton and/or deuteron acceleration at defined particle energies, while research cyclotrons can accelerate other particles, such as protons, deuterons, <sup>3</sup>He, or <sup>4</sup>He, over a wide energy range despite the fact that the fundamentals of cyclotron technology have not changed since the early 1930s, significant advancements in the RF system and target technology, for instance, have led to the development of extremely potent medical cyclotrons. Medical cyclotrons are characterized by proton only or proton and/or deuteron acceleration at defined particle energies, while research cyclotrons can accelerate other particles, such as protons, deuterons, <sup>3</sup>He, or <sup>4</sup>He, over a wide energy range.

The transformation of radioisotopes produced by cyclotrons into more complex compounds of interest is necessary for the medical application of positron emitters. However, in order to produce enough radiotracer for the medical application, substantial quantities of the applicable radioisotopes must be manufactured and handled due to their short physical half-life. Large-scale radioactive waste management calls for automated methods in protected settings. The earliest automation systems were typified by the use of standard remotely operated chemistry laboratory apparatus; however, more advanced and adaptable automation quickly followed with the introduction of desktop computers and programmable logic controllers (PLC). Pharmaceuticals, or radiopharmaceuticals, have to be made in a GMP-regulated facility. GMP was first implemented in the EU in 1992 and has since been continuously improved. Production demands grew as a result of stricter GMP regulations. Although in the past "open" production devices were typical, manufacturing is increasingly going to be done in closed, separated systems. The updated EU GMP Annex 1, which governs the aseptic production of medications, is anticipated to go into force in the fall of 2021. There will be new requirements for the production of radiopharmaceuticals as a result of the updated Annex 1.

### Creation of radionuclides

#### Physical foundation

Artificial radionuclides typically need to be created through a nuclear reaction in

which a lighter nuclear bullet bombards the target nucleus of an element (Fig. 1). Usually, a nuclear reaction involving the bombardment of an element's target nucleus by a lighter nuclear bullet is required to produce artificial radionuclides (Fig. 1). The reaction will typically fragment into two product nuclei with varying weights, with the product of interest typically making up the heavier part. A charged particle from an accelerator, such as a proton (p), deuteron (d), or neutron (n) from a nuclear reactor, can be the projectile. This can produce products that are typically either neutron-rich or neutron-deficient. Reactor-based generation is irrelevant for PET because positron emission radioactive decay is limited to radionuclides that lack neutrons.

In order to overcome the electrostatic repulsion between the positively charged projectile and target nucleus, which can range from 2 to 10 MeV for light to heavy target nuclei, using a charged particle as the projectile in a nuclear reaction requires kinetic energy beyond a particular threshold. The reaction's so-called Q-value, which is exclusively based on the atomic mass of the particles involved, plays a significant role in determining the energy threshold. Depending on the selected nuclear reaction, the precise yield of a given product may differ significantly even after the energy threshold requirement is met.

Using a typical "medical cyclotron," a variety of radionuclides are frequently produced for PET. Table 1 lists some of the most often used radionuclides along with a few physical characteristics that are important for



Short nomenclature:  $A(a,b)B$

**Table 1 Most commonly used radionuclides for PET with relevant decay data**

Nuclide	Half-life	Max positron energy (MeV)	$\beta^+$ branching ratio (%)	Production
$^{11}\text{C}$	20.4 min	0.96	99	Cyclotron
$^{13}\text{N}$	9.96 min	1.19	100	Cyclotron
$^{15}\text{O}$	2.04 min	1.72	100	Cyclotron
$^{18}\text{F}$	110 min	0.635	97	Cyclotron
$^{68}\text{Ga}$	67.7 min	1.90	89	Cyclotron, generator
$^{64}\text{Cu}$	12.7 h	0.653	17.6	Cyclotron
$^{89}\text{Zr}$	78.4 h	0.902	22.7	Cyclotron

**Figure 1** Nuclear reaction where target nucleus A is bombarded with beam particle a, resulting in the product nucleus B.

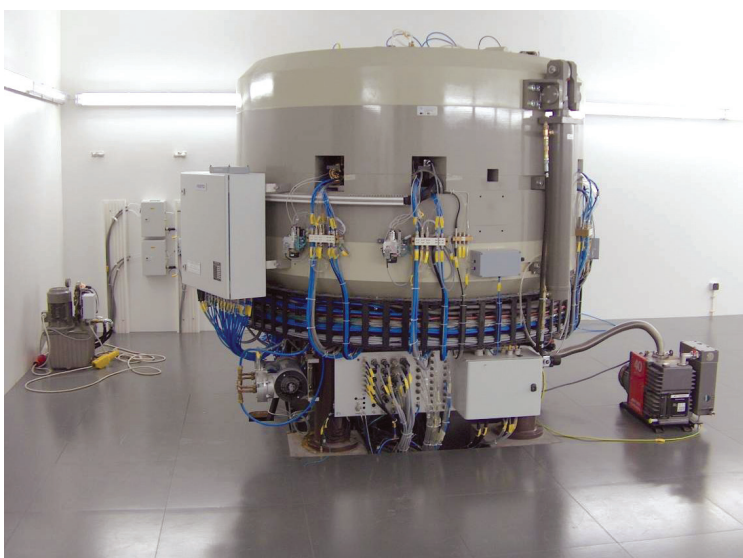
PET imaging. The physical half-life is crucial because it establishes the time-scale for the biological phenomena that can be studied by limiting the amount of time available for tracer synthesis and imaging. Since a low positron branching ratio will need to be made up for by increasing the injected activity and thus the dose contribution from competing decay modes like electron capture or  $\beta^-$  emission, the positron branching ratio primarily affects the relationship between the dose burden to the patient and the achievable image quality (signal and/or noise ratio). Similarly, a high energy positron emission will result in a higher radiation dosage and a slight reduction in spatial resolution because of the greater positron range before annihilation. The potential presence of extra gamma rays released in cascade with the positrons, which could result in the simultaneous generation of multiple photons and uncertainty regarding the unambiguous detection of the two paired annihilation photons, is a final factor to take into account when selecting a radionuclide for PET studies. These "non-pure" radionuclides may cause extra gamma rays, which could impair image quality and add to the previously mentioned dose load. Table 1 lists the radionuclides that are thought to be pure positron emitters, with the exception of  $^{68}\text{Ga}$ , which decays by emitting a prompt gamma ray with a mass of 1077 keV.

All of the radionuclides listed in Table 1 can be created using a cyclotron; however, the majority of  $^{68}\text{Ge}$  production occurs in

a small, straightforward  $^{68}\text{Ge}/^{68}\text{Ga}$  generator, where  $^{68}\text{Ga}$  is continually produced through the 270-day half-life decay of the parent radionuclide  $^{68}\text{Ge}$ . The  $^{82}\text{Sr}/^{82}\text{Rb}$  generator, which produces the extremely short-lived  $^{82}\text{Rb}$  mostly used for cardiac perfusion imaging, operates similarly.

### Cyclotrons

As shown in Table 2, cyclotrons specially created and tuned for the synthesis of PET radionuclides are currently offered for sale by a number of vendors in a range of sizes. Overall, the progress of cyclotron technology has been characterized by a continual concentration on automation, reliability enhancement, and raising the maximum beam current to increase production capacity rather than any significant technological breakthroughs. The key distinctions among the models are mostly related to





**Table 2** Commercially Available Cyclotrons Developed for Production of PET Radionuclides

Manufacturer	Model	Beam	Dual beam	Protons		Number of targets
				<i>E</i> (MeV)	<i>I</i> <sub>max</sub> (μA)	
GE Healthcare	GENtrace	p	No	7.8	35	1
	MINItrace	p	No	9.6	70	5
	PETtrace 800	p,d	Yes	16.5	160	6
Advanced Cyclotron Systems	TR19	p,d	Yes	14-19	300	8
Ion Beam Applications	Cyclone Kiube	p	Yes	18	300	8
Best Cyclotron Systems	Best 15p	p	Yes	15	400	4
	Best 6-15p	p	Yes	6-15	1000	4
Best ABT Molecular Imaging	BG-75	p	No	7.5	5	3
Nucletron MIT	Ionetix ION-12SC	p	No	12	25	1
PMB	iMiTRACE	p	No	12	50	4

Information listed is gathered from publicly available product information or from the companies homepage.

the delivered ion beam's performance parameters, the deuteron beam's optionality, the models' adaptability to the simultaneous bombardment of many targets, and the different degrees of integrated chemical precursor processing. The firms provide a wide range of optional targets, such as producing radionuclides such as <sup>11</sup>C, <sup>13</sup>N, <sup>15</sup>O, <sup>18</sup>F, <sup>64</sup>Cu, <sup>68</sup>Ga, <sup>89</sup>Zr, <sup>99m</sup>Tc, and <sup>124</sup>I.

The maximum beam current that is available, which for current systems is in the range of 25-1000 mA, mostly determines the production rate. Additionally, the achievable production rate can be greatly influenced by the beam energy, especially when producing radionuclides of heavier elements with larger threshold energies. Higher beam energy, however, can also force a necessary restriction on the applied beam current because of the target's restricted cooling capacity and power dissipation.

The ability to install several targets (1–8) and the potential for dual-beam extraction to allow for the simultaneous bombardment of two targets offer the flexibility of daily production. In order to attain high production rates at maximum beam currents, such as for large-scale production of <sup>18</sup>F, dual bombardment of two targets is typically envisaged.

Traditionally, cyclotrons and other accelerators have been housed in concrete bunkers to ensure protection from the ra-

diation created during operation. This has resulted in significant space requirements and installation expenses. Furthermore, the expenses associated with the facility's eventual decommissioning owing to neutron activation of the building's structure and different cyclotron components might be high and on par with the establishment expenditures. All of the cyclotrons in Table 2, with the exception of the Cyclone Kiube and Best <sup>15</sup>p, can be placed with variable degrees of integrated radiation shields, which will reduce future costs associated with decommissioning building components. Compared to a freestanding cyclotron in a bunker, the integrated radiation barrier may, in some cases, make it more difficult to access certain machine parts.

The availability of small, self-shielded cyclotrons with low beam energy and maximum beam current is one of the most recent advancements in PET cyclotron technology. These cyclotrons not only offer lower power consumption but also significantly lower installation and decommissioning costs. These devices are meant for small-scale production, but they might potentially be installed next to the scanner suite for manufacturing at the bedside, such as [<sup>15</sup>O] water. The introduction of cyclotrons with variable beam energy, such as the TR19 or the Best 6-<sup>15</sup>p, is another intriguing development. The ability to optimizeradionuclide purity—for instance, during <sup>68</sup>Ga synthesis, where

the contaminant  $^{67}\text{Ga}$  can be regulated by reducing the applied beam energy—is a significant advantage of a variable beam energy. More generally, improving beam energy may enable an increase in beam current and, consequently, the yield within the target's allowable maximum power dissipation.

### Progress in the Manufacturing of Tracers $^{15}\text{O}$

The applications of  $^{15}\text{O}$ -labelled compounds are limited to simple, readily available molecules such as  $[^{15}\text{O}]\text{H}_2\text{O}$  and gases like  $[^{15}\text{O}]\text{CO}$  and  $[^{15}\text{O}]\text{CO}_2$ , due to their short half-life of 2.04 min. The production of more intricate compounds, such as 6- $[^{15}\text{O}]$ -2-deoxy-glucose, was merely experimental evidence. Particularly,  $[^{15}\text{O}]\text{H}_2\text{O}$  is widely used as a perfusion tracer. In medical cyclotrons, the nuclear reactions  $^{14}\text{N}(\text{d},\text{n})^{15}\text{O}$  and  $^{15}\text{N}(\text{p},\text{n})^{15}\text{O}$  are used to make  $^{15}\text{O}$ . Both strategies need the addition of stable  $\text{O}_2$ , which lowers the final radiopharmaceuticals' molar activity.  $[^{15}\text{O}]\text{O}_2$  can be created in a cyclotron in a single batch or constantly, with the formed  $[^{15}\text{O}]\text{O}_2$  being continually extracted from the target in a predetermined target gas flow. In any event, using enriched nitrogen-15 as the target gas results in a noticeable cost difference, and recovering nitrogen after radiation should be taken into account. The most common method of producing  $[^{15}\text{O}]\text{H}_2\text{O}$  is catalytically burning  $[^{15}\text{O}]\text{O}_2$  with hydrogen. Owing to the brief half-life, bedside manufacturing next to the scanner is now the preferred method of producing  $[^{15}\text{O}]\text{H}_2\text{O}$ . In this instance, the cyclotron's mixture of  $[^{15}\text{O}]\text{O}_2$  and hydrogen gas is transformed into  $[^{15}\text{O}]\text{H}_2\text{O}$ , trapped in a physiological sodium chloride solution in water for injection, and then automatically given to the patient. The operator's radiation exposure is kept to a minimum, and the studies are carried out in a very reproducible and standard manner. It should be mentioned that this method requires a

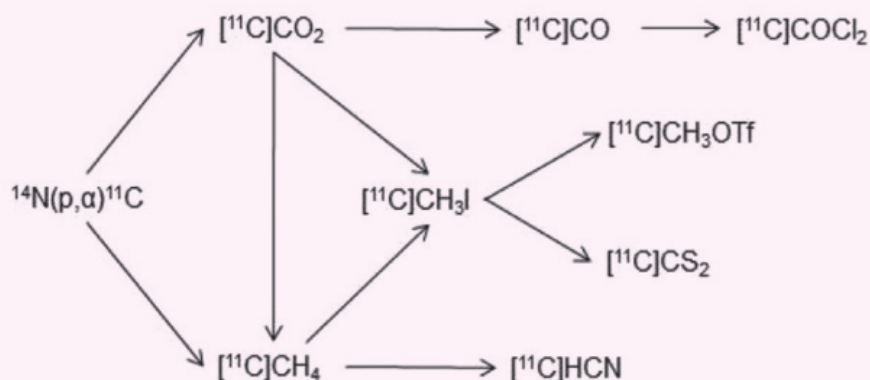
cyclotron because, absent additional cyclotron capacity, no further radioisotope manufacturing could be carried out during the water perfusion investigations.

### $^{13}\text{N}$

Particularly,  $[^{13}\text{N}]\text{ammonia}$  was used in heart perfusion experiments conducted between the late 1990s and the mid-2000s. The application of  $[^{13}\text{N}]\text{NH}_3$  in quantitative perfusion experiments is fairly limited because of the considerably greater perfusion properties of  $[^{15}\text{O}]\text{H}_2\text{O}$ . In  $\text{H}_2^{16}\text{O}$  water targets, the  $^{13}\text{N}$  reaction ( $^{16}\text{O}(\text{p},\text{n})^{13}\text{N}$ ) produces  $^{13}\text{N}$ . The main precursors in target are  $[^{13}\text{N}]$  nitrate and nitrite, which are reduced to  $[^{13}\text{N}]\text{ammonia}$  either outside of target by Devardas alloy or in target in the presence of trace amounts of ethanol. It is important to consider radionuclidic purity while applying in-target production. In addition to being utilized as a perfusion tracer,  $[^{13}\text{N}]\text{ammonia}$  was also employed as a metabolic tracer, particularly in the study of hepatic encephalopathy. While  $[^{13}\text{N}]\text{ammonia}$  is the most commonly used  $^{13}\text{N}$ -labelled radiotracer, there have been reports of the production of more sophisticated radiotracers such as  $[^{13}\text{N}]\text{Nifedipine}$  and the amino acid  $^{13}\text{N}$ -L-glutamate. The 9.96 min physical half-life is a limiting factor, though, just like it is for  $^{15}\text{O}$ .

### $^{11}\text{C}$

Almost all compounds that are important to human health contain the elements carbon, nitrogen, and oxygen. This implies that an astounding number of molecules might be radioactively labelled with these elements without undergoing any alterations. The production of more complicated chemicals and the execution of more complex PET procedures are made possible by the 20.4 min half-life of carbon-11, while automated manufacture and PET scanning processes are limited by the 2.04 min ( $^{15}\text{O}$ ) and 9.96 min ( $^{13}\text{N}$ ) half-lives. As a result,  $^{11}\text{C}$  is currently among the most interesting



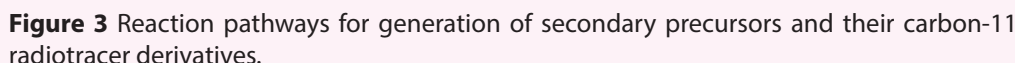
**Figure 2** Secondary labelling precursors with carbon-11 chemistry

PET isotopes for scientific study  $^{11}\text{C}$  is created in gas targets by the nuclear reaction  $^{14}\text{N}(\text{p}, \alpha) ^{11}\text{C}$ . When oxygen is added to the target gas,  $^{11}\text{C}$  is either recovered as  $^{11}\text{C}\text{CO}_2$  or as  $^{11}\text{C}$ -methane when hydrogen is added. Targeting receptors for PET studies often aims to minimize the applied amount of radiotracer in order to avoid interfering with physiological circumstances. The molar activity is the expression for this quality metric. Molar activity, traditionally known as specific radioactivity, is the ratio of a labelled to an unlabeled chemical. The amount of the greenhouse gas carbon dioxide in the atmosphere is always rising, hence significant efforts are needed to produce radiotracers that have a high molar activity. When generating  $^{11}\text{C}$ -methane, larger molar activities are attained due to the significantly reduced methane content. However,  $^{11}\text{C}$ -methane is more susceptible to radiolysis than  $^{11}\text{C}\text{CO}_2$ , and significant radioactive target losses are noted. As a result, only roughly one-third as much  $^{11}\text{C}$ -methane as  $^{11}\text{C}\text{CO}_2$  is generated. Methane and carbon dioxide, the primary labelling precursors  $^{11}\text{C}$ , are further transformed, frequently in real time, to secondary labelling precursors right after the end of cyclotron production (Fig. 2). By using these secondary labelling precursors,  $^{11}\text{C}$  can be applied to practical-

ly any organic molecule. Owing to its brief half-life, radiolabeling is typically done as the final step in a one-step labelling process. Several hundred distinct compounds were labelled using  $^{11}\text{C}$ -methyl iodide, the most widely used precursor for secondary labelling. The development of  $^{11}\text{C}$ -methyl triflate as a methylation reagent was a breakthrough in  $^{11}\text{C}$  methylation procedures. The use of methyl triflate, for example, expands the spectrum of solvents in methylation processes and hence widens the possibilities for sequential reactions because of the approximately 10,000 times higher reactivity. The development of  $^{11}\text{C}$ -methyl iodide synthesis in the so-called "gas phase" was another important breakthrough in  $^{11}\text{C}$  labelling. <sup>37</sup> Here, iodine and methane react at a high temperature in a closed system. When this method is used instead of the traditional reduction of  $^{11}\text{C}\text{CO}_2$  with lithium aluminum hydride and acidolysis with hydroiodic acid, much greater molar activity are obtained. An advancement in  $^{11}\text{C}$  methylation techniques was the creation of  $^{11}\text{C}$ -methyl triflate as a methylation reagent. Because of its roughly 10,000-fold higher reactivity, methyl triflate, for instance, broadens the range of solvents that can be used in methylation operations, increasing the potential for subsequent reactions. Another key advance in  $^{11}\text{C}$  labelling was the creation of  $^{11}\text{C}$ -methyl iodide syn-



Notable in this instance is the SV2A ligand [ $^{11}\text{C}$ ]-UCBJ. Carbon monoxide is a fundamental component of medicinal chemistry, and the use of [ $^{11}\text{C}$ ]CO has resulted in significant advancements in the synthesis of molecules labelled with  $^{11}\text{C}$ . The early experiments required high pressure carbonylation reactors because carbon monoxide was poorly soluble in organic solvents; however, more practical pressure approaches are now available. Not only may  $^{11}\text{C}$  labelling be used for substances that target receptors, but it can also be used for metabolic tracers like as glucose, methionine, choline, and acids like acetic and palmitic acid. Despite the remarkable potential of  $^{11}\text{C}$  compounds in research, there is not much clinical applicability for these molecules.



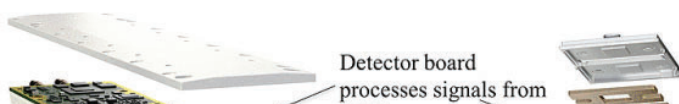
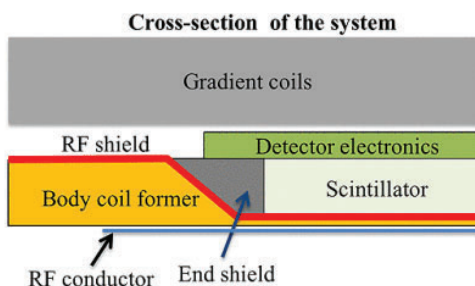
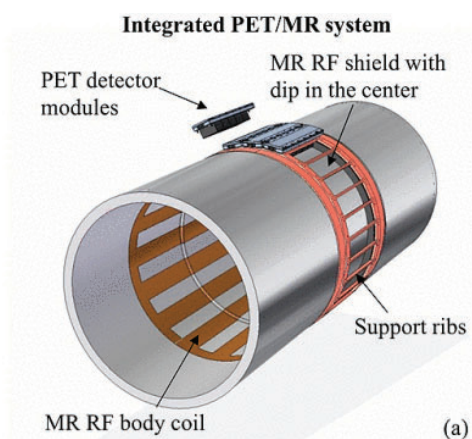
Owing to its 20.4 minute half-life, a production can frequently only withstand one inspection. However, there are instances of repeated tests using batches of [ $^{11}\text{C}$ ]-choline or -methionine. Notwithstanding these limitations,  $^{11}\text{C}$ -labeled molecules for clinical use could be a more affordable option in smaller facilities with less stringent testing needs.

The primary carbon-11 precursors like, such as [ $^{11}\text{C}$ ] $\text{CO}_2$  and [ $^{11}\text{C}$ ] $\text{CH}_4$ , are converted transformed into secondary precursors by rapid via quick and efficient effective online or one-pot synthetic procedures to produce building blockers for generating carbon-11 radiotracers. There processes. To create secondary antecedents, there are several useful numbers of helpful transformations for the generation. Many of the possible radiotracers are produced from a variety of secondary precursors. Many of the potential radiotracers are generated using various secondary precursors, which include [ $^{11}\text{C}$ ]- such as [ $^{11}\text{C}$ ] raclopride (an antagonist of the brain  $\text{D}_2/\text{D}_3$  receptor) from  $^{11}\text{CO}$  precursor and [ $^{11}\text{C}$ ] flumazenil (GABAA benzodiazepine receptors) from  $^{11}\text{CH}_3\text{I}$  precursor, [ $^{11}\text{C}$ ] raclopride (cerebral  $\text{D}_2/\text{D}_3$  receptor antagonist) from  $^{11}\text{CO}$  precursor, precursor the compounds  $^{11}\text{C}$ (carbonyl)-estramustine phosphate (estrogen agonist for the estrogen receptor agonist) from  $^{11}\text{COCl}$  precursor, [ $^{11}\text{C}$ ] thymidine (pyrimidine derivative for DNA synthesis) from  $^{11}\text{COC}_2$  precursor, [ $^{11}\text{C}$ ] citalopram (selective serotonin reuptake inhibitor) from  $^{11}\text{CN}$  precursor, [ $^{11}\text{C}$ ] serine (synaptic N-methyl-D-aspartate receptors) from  $^{11}\text{CH}_2\text{O}$  precursor, [ $^{11}\text{C}$ ] tanaproget (selective progesterone receptor modulator) from  $^{11}\text{CS}_2$  precursor, and [ $^{11}\text{C}$ ] NS14492 ( $\alpha 7$ -subtype nicotinic Ach receptor agonist) from  $^{11}\text{CH}_3\text{OTf}$  precursor (Figure 3).

#### $^{18}\text{F}$

The most significant and often utilized PET isotope, or the "work horse" in clinical PET, is  $^{18}\text{F}$ . Normally, the  $^{18}\text{O}(\text{p},\text{n})^{18}\text{F}$  reaction is used to irradiate enriched O-18 water in order to make  $^{18}\text{F}$ . Many hundred GBq of  $^{18}\text{F}$  may be reliably produced by this extremely ef-

fective nuclear reaction, which may be easily dissolved to produce [ $^{18}\text{F}$ ]fluoride. Using the nuclear reactions  $^{20}\text{Ne}(\text{d},\text{a})^{18}\text{F}$  or  $^{18}\text{O}(\text{p},\text{n})^{18}\text{F}$  reaction in  $^{18}\text{O}$ -gas targets are alternative manufacturing routes. Only [ $^{18}\text{F}$ ]fluorine gas for use in electrophilic fluorinations is delivered by the last two processes. For molecules labelled with [ $^{18}\text{F}$ ] $\text{F}_2$ , the molar activity is significantly lower because fluorine recovery from the target requires the injection of non-radioactive [ $^{19}\text{F}$ ]fluorine gas. In addition to the very effective nuclear reaction, the handy half-life of 109.8 minutes permits advanced chemical processes and transportation to different locations. Sodium fluoride [ $^{18}\text{F}$ ]NaF is the most basic  $^{18}\text{F}$  radiotracer and can be used to identify bone metastases. 2-[ $^{18}\text{F}$ ] Fluoro-2-deoxy-glucose is the most significant and widely utilized PET tracer (FDG). Since the manufacturing of [ $^{11}\text{C}$ ]-glucose is somewhat labor-intensive, FDG has been utilized as a temporary substitute for glucose metabolism imaging since the advent of PET technology. The initial method used to react fluorine gas with glucal produced very little of this tracer with poor molar activity. Using a nucleophilic substitution process in protected mannose triflate with amino polyether activation of [ $^{18}\text{F}$ ]-fluoride, a significant advance was made towards the end of the 1980s. Large amounts of FDG could be produced with this manufacturing process. Several hundred GBq of GMP-compliant product are produced in less than 30 minutes with the help of additional chemical development and the creation of authorized production equipment. In addition, handling such high levels of radioactivity led to the creation of specialized dispensing equipment that was previously unavailable. There are very few other  $^{18}\text{F}$  labelled tracers that have had a significant clinical impact aside than FDG. These drugs target tau and b-amyloid; several of the candidates were produced by commercial corporations.  $^{18}\text{F}$  labelled choline derivatives, [ $^{18}\text{F}$ ]Fluoroethyl tyrosine, [ $^{18}\text{F}$ ]Fluoro-30 -deoxy-30 -L-fluorothymidine, and [ $^{18}\text{F}$ ]FDOPA55 are interest-



ing radiotracers for cancer applications, but they were never widely used. At now, [ $^{18}\text{F}$ ] FPSMA-1007, is the radiotracer that has the most promise for broad usage.

A shift from so-called fixed tube synthesis modules, such as GE Healthcare Figure 2 Secondary labelling precursors with carbon-11 chemistry, was observed in terms of automation starting about 2000. There was a shift from Tracerlab FX-FN to cassette-based systems, such as GE 270 S.B. Hansen and D. Bender Healthcare Fastlab or ORA-Neptis. Whereas the cassette-based systems lack the ability for HPLC purification, at least in their initial iterations, they are reliant on chemical kits and cassettes unique to the tracer, while the fixed tube systems offer a great deal of versatility and flexibility. Nevertheless, with current developments, cassette-based systems also incorporate radio-HPLC. Moreover, as automation advanced, GMP components became increasingly integrated, reflecting the need for production that complies with GMP standards.

### $^{68}\text{Ga}$

In the beginning,  $^{68}\text{Ga}$  was employed for imaging as [ $^{68}\text{Ga}$ ]-EDTA or even [ $^{68}\text{Ga}$ ]-citrate. Comparable simple complexation with appropriate chelators is the quick chemical step

used for  $^{68}\text{Ga}$  labelling. As a result, lengthy processes like those in the  $^{18}\text{F}$  chemistry are avoided. Moreover, the final labelling step enables the creation of radiopharmaceuticals that are equivalent to those that are known from containing  $^{99\text{m}}\text{Tc}$  compounds.  $^{68}\text{Ga}$  is most commonly obtained using  $^{68}\text{Ge}/^{68}\text{Ga}$  generators, which provide cyclotron independent  $^{68}\text{Ga}$  availability. One drawback is the extremely low  $^{68}\text{Ga}$  radioactivity following elution, which even goes down over the generator's lifetime. The primary drawback of  $^{68}\text{Ge}/^{68}\text{Ga}$  generators can be addressed by producing  $^{68}\text{Ga}$  internally using a cyclotron, either by irradiating  $^{68}\text{Zn}$  solid targets 60 or  $^{68}\text{Zn}$  solutions in liquid targets. With the possibility of daily supplies of  $^{68}\text{Ga}$  for radio-labelling, especially solid targets can produce massive volumes of  $^{68}\text{Ga}$  and thus provide an alternative to generators even for sites without cyclotron.

Peptide-based tracers that target neuroendocrine tumors (TOC, NOC, and TATE) have made a comeback and made  $^{68}\text{Ga}$  a widely utilized PET isotope. [ $^{68}\text{Ga}$ ]-PSMA-1163 was a significant development in the field of  $^{68}\text{Ga}$  labelled chemicals, alongside TOC, NOC, and TATE. The most talked about  $^{68}\text{Ga}$  radiotracer at the moment is [ $^{68}\text{Ga}$ ]FAPI

**See Next issue**





## ROBOTICS IN INTERVENTIONAL RADIOLOGY AND SURGERY

**Jasveer Singh**, Research fellow;

**Viswanath Pratap Singh**, Assistant Professor, Radio-imaging

Department of Paramedical Sciences, Swami Vivekanand Subharti University, Meerut,  
College of Paramedical Sciences, Teerthanker Mahaveer University, Moradabad, UP

**R**obotic technology has made remarkable strides in the medical field, particularly in interventional radiology and surgery. Over the past few decades, robots have been increasingly integrated into medical procedures to augment the capabilities of healthcare professionals, minimize invasiveness, and improve patient outcomes. This paper provides an in-depth analysis of robotic systems in interventional radiology and surgery, focusing on their evolution, current applications, challenges, and the promising future they hold (Carolina Lanza, 2023).

### ◆ **Conduct minimally invasive biopsy procedures:**

This can be less invasive and more precise than

conventional open biopsy procedures. This novel method for identifying cancer and other disorders has the potential to be very effective.

### ◆ **Real-time imaging with robotic surgery:**

Real-time imagery of the surgical site can be provided through robotic surgery, which can assist doctors in making better informed choices during surgery. Improved accuracy and patient outcomes may result from this.

### ◆ **The application of augmented reality in robotic surgery:**

Augmented reality may be utilized in robotic surgery to assist doctors see more clearly and interact with the operative site more accurately. Improved accuracy and patient outcomes may result

from this.

### ◆ **The use of robotic surgery in the education of surgeons:**

Minimally invasive surgical procedures may be taught to surgeons through the use of robotic surgery. This could aid in enhancing surgeons' abilities and lowering the incidence of postoperative problems.

## **ROBOTICS IN INTERVENTIONAL RADIOLOGY**

### **1. Robotically guided MRI and CT procedures:**

Since CT and MRI both provide three-dimensional imaging of any location of the body at relatively high resolutions, they were the logical starting points for robotic guided procedures. (SMori,2023) Although CT guided interventions are widely known, the drawbacks of radiation exposure, confined tunnel dimensions, several steps required to position the needle, and planning that takes place outside the scan room make operations time-consuming. Due to the expense, the size of the tunnels, and the limitations on the devices that may be utilized, MR guided interventions are less well established.

### **2. Robot-guided ultrasound procedures:**

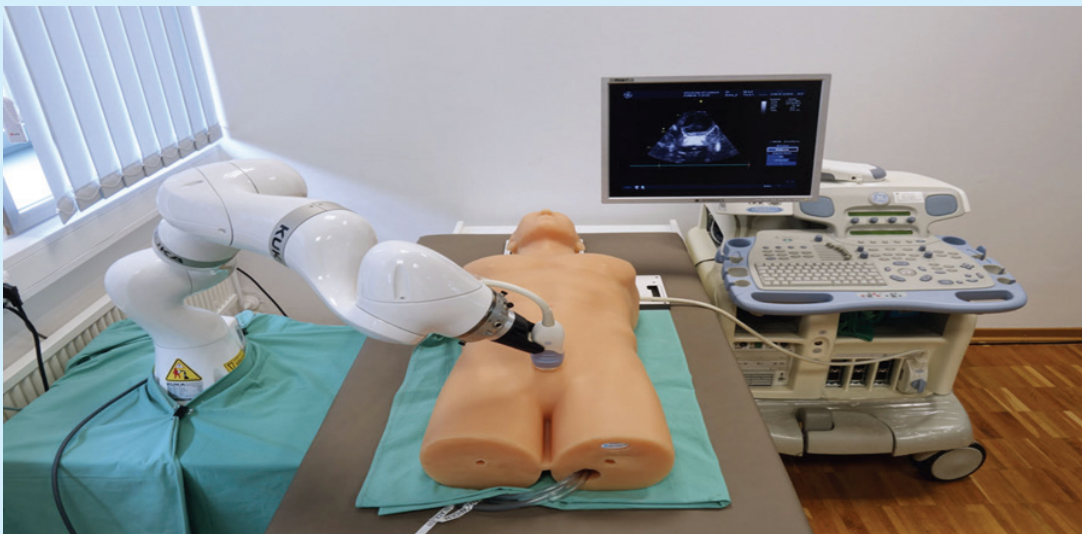
Because two-dimensional ultrasonic imaging is so operator-dependent, robot advancement in this field has lagged. Tissue motion analysers, however, can be used by robots to guide needles into specific trajectories provided a predetermined trajectory is recognized and the location of the

ultrasound probe is stabilized. The Da Vinci robot is already used in conjunction with transrectal ultrasonography (TRUS) for prostatectomy. With the goal of minimizing problems, the TRUS enables visualization of the instrument tips, dissection planes, bladder neck, and neurovascular bundle.

### **3. Robot fluoroscopy guided procedures:**

Initially used to position catheters during cardiac ablations, robotic catheter steering devices were later modified for use during percutaneous coronary intervention (PCI). Accurate lesion estimations, exact stent insertion, decreased radiation exposure, and reduced contrast supply are some potential advantages for patients. Additionally, their approach utilized a robotic arm for cannulation. There have been post-interventional problems with this procedure, which has only been employed in restricted clinical settings. Their research demonstrated how the robotic system allowed for precision vessel manipulation, placement, and minimal instrumentation while reducing operator radiation exposure. Additionally, it was shown that the robotic arm for cannulation speeds up vascular cannulation.

Due to its two-dimensional nature, biplanar fluoroscopy is not as well suited for robotic treatments as CT and MRI. The AcuBot is a robot that can do fluoroscopic treatments and has shown to be accurate when injecting facet joints and the peri spinal nerve.



*Robots take ultrasound to the fourth dimension*

#### 4. Robotic endovascular procedures:

Due to its two-dimensional nature, biplanar fluoroscopy is not well suited for robotic treatments like CT and MRI. The AcuBot is a robot that can do fluoroscopic treatments and has shown to be accurate when injecting facet joints and the peri spinal nerve.

### ROBOTICS IN SURGERY

#### 1. Robotic Gynecologic Surgery:

Robotic gynecologic surgery may be a good substitute for open surgery or common laparoscopic treatments for some women. The traditional method for gynecologic treatments for many years has been open gynecologic surgery, in which a large incision is created in the abdomen to provide a surgeon access to the uterus and surrounding anatomy. Open surgery, however, can result in substantial pain, physical stress, and a protracted recovery period. (H Schoellnast, 2019) Smaller incisions that may cause less post-operative pain, less blood loss and a lesser need for blood transfusions, as well as a potential for a quicker recovery and return to normal activities, are some potential benefits of laparoscopic and robot-assisted laparoscopic hysterectomy and other gynecologic procedures over open surgery.

#### 2. Robotic Prostate Surgery:

Studies show that radical prostatectomy, or the surgical removal of the prostate and any nearby malignant tissues, is one of the most successful therapies for prostate cancer. US surgeons often employ one of three techniques: open surgery (which necessitates a significant abdominal incision), laparoscopic surgery, or robotic-assisted laparoscopic surgery. The surgeon's objective is always the same: to separate the prostate gland from the surrounding tissue, regardless of the surgical technique.

#### 3. Robotic Kidney Surgery:

The kidneys are two fist-sized organs that are situated immediately below the rib cage, in the center of the back. Urine is produced when waste materials and surplus water are removed by the kidneys. The bladder receives the urine through tubes known as ureters. (H Ahmed, 2021) Numerous disorders, such as diabetes, hypertension, cancer, cysts, stones, and infections, can harm the kidneys. Chronic renal disorders can also be brought on by genetic issues, accidents, and medications.

#### 4. Robotic Colorectal Surgery:

A robotic colectomy involves the removal of benign tumors and polyps in addition to malignant sections of the colon and rectum. After the cancer

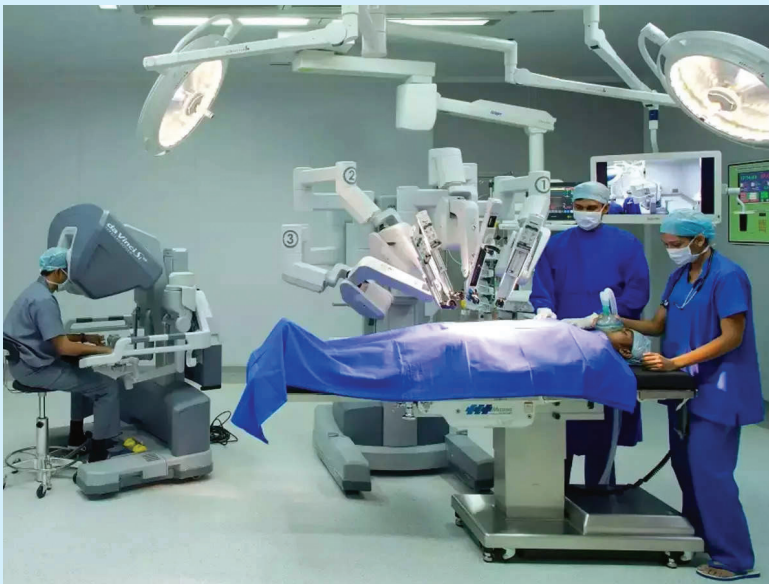
has been removed, a robot-assisted technique gives surgeons the tools they need to join the two ends of the colon more quickly. (E Khoury, 2021) Instead of the single lengthy incision required in conventional open colon surgery, the treatment can be accomplished with a few minor incisions.

#### ●Research using robotic surgery:

Research on novel surgical methods and technology may be done using robotic surgery.

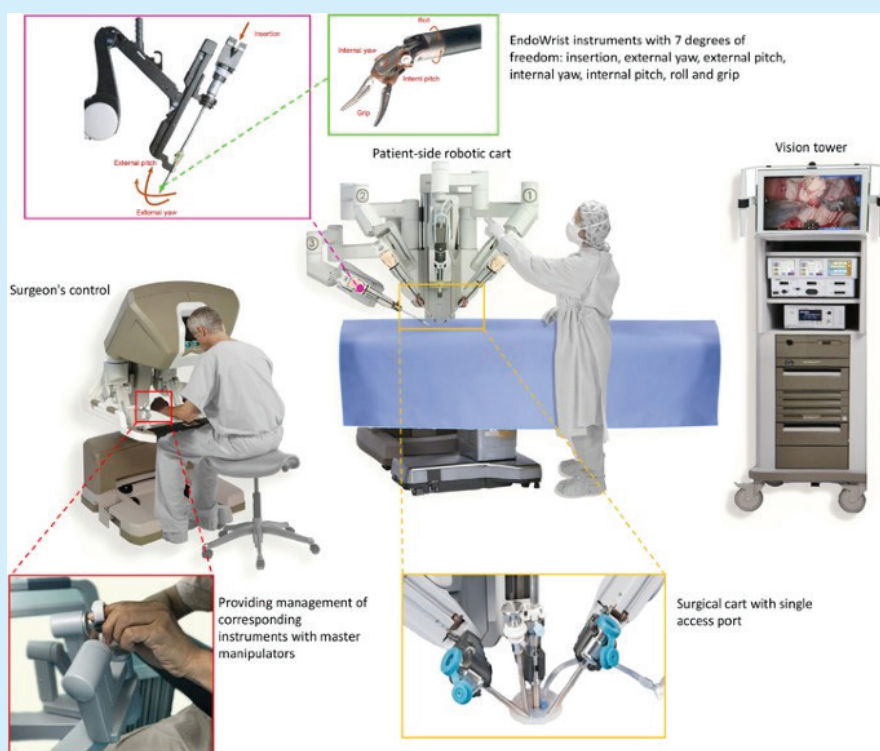
#### ●Targeted Cellular Diagnostics Using Nanorobotics in Robotic Surgery:

This subject explores the cutting-edge discipline of nanorobotics and its application



*Robotic surgery room design*





*Robotic surgical systems*

to focused cellular diagnosis in robotic surgery. It goes into how nanorobots may be created to distribute contrast chemicals, gather tissue samples, and do in-the-moment cellular analysis, possibly transforming the early diagnosis and treatment of illness.

### ● **Balancing Automation and Human Diagnostic Skill: Ethical Considerations in Robotic Surgery:**

The ethical issues raised by the growing use of robotic technologies for surgical diagnostics are examined in this topic. It examines how automation could coexist with the requirement for human skill in evaluating diagnostic data offered by robotic technologies. The abstract could go over patient permission, responsibility, and the significance of human judgment.

### ● **Evolution of Robotic Systems in Medicine:**

The inception of robotic systems in medicine dates back to the late 20th century, with the development of the first robot-assisted surgical system, the PUMA 560. Since then, numerous advancements have occurred, leading to the emergence

of highly sophisticated robotic platforms, such as the da Vinci Surgical System. This section provides a historical overview of the evolution of robotic systems in medicine, highlighting key milestones and breakthroughs.

### ● **Technical Aspects of Robotic Systems:**

To understand the capabilities and limitations of robotic systems in interventional radiology and surgery, it is crucial to delve into their technical aspects. Topics covered in this section include the robotic arm design, control systems, sensors, imaging integration, and haptic feedback. A thorough understanding of these technical components is essential for medical professionals and researchers working with robotic platforms.

## **MATERIAL AND METHOD**

### ● **System components for robot:**

A robotic system is made up of a number of essential parts for its operation. The main components of a robotic system, such as robotic arms, end-effectors, sensors, imaging modalities, and control interfaces, are described in this section.



Understanding these elements is necessary to grasp the tools and processes that make robotic interventions possible.

### ● **Surgical instrument materials:**

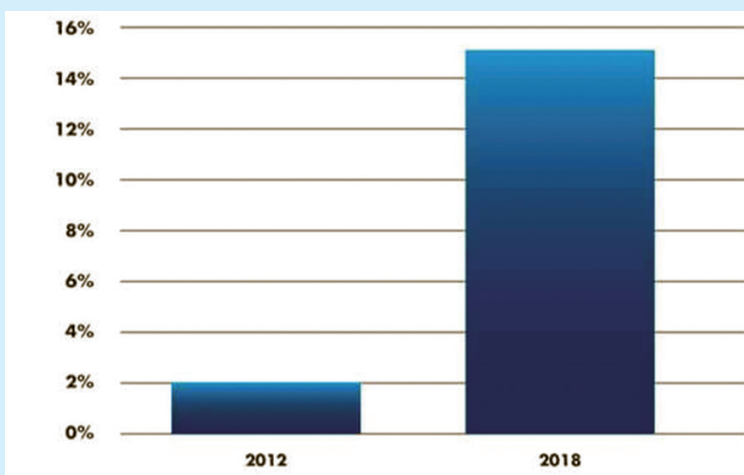
In order to perform accurate and less invasive surgeries, robotic surgical tools are essential. The components needed to make robotic surgical instruments, including laparoscopic instruments and robotic catheters, are examined in this section. To guarantee patient safety, sterilizing methods, biocompatible materials, and coatings are reviewed.

### ● **Technical Approaches and Control Techniques:**

Robotic systems rely on complex technological procedures and control systems to function. This section explores the techniques for haptic feedback, real-time imagery integration, and robotic motion control. Additionally, it examines how software and algorithms help to facilitate accurate and dynamic motions throughout processes.

### ● **Maintaining and Sterilizing:**

In medical settings, maintaining a sterile surgical environment is crucial. The methods and supplies required to sterilize robotic component parts are covered in this section to guarantee their cleanliness and safety. The use of routine maintenance procedures is also being investigated to increase



Percentage of robotic surgery and procedure

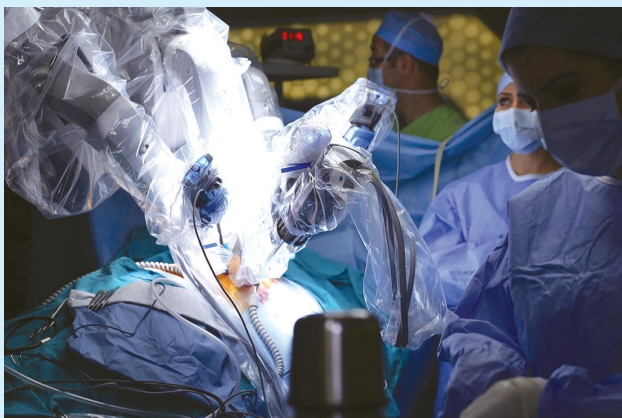
the longevity of robotic systems.

### **BENEFITS AND ADVANTAGES**

The integration of robotic technology into medical practice brings several benefits and advantages. These include enhanced precision, reduced invasiveness, shorter recovery times, and improved patient safety. We discuss these advantages in detail, presenting empirical evidence from clinical studies and patient testimonials that highlight the positive impact of robotic systems on healthcare.

### **CONCLUSION**

An innovative age in the area of medical interventions has begun with the use of robots into interventional radiology and surgery. The integration of state-of-the-art robotics technology with the knowledge of knowledgeable medical professionals has produced amazing improvements in precision, safety, and patient outcomes, as illustrated throughout this extensive study. Robotic systems have proven they are capable of navigating intricate anatomical structures with unmatched accuracy, lowering the risk of mistake and limiting injury to healthy tissue. Additionally, they have improved the dexterity of interventional radiologists and surgeons, enabling them to carry out complex treatments that were previously thought to be impossible.

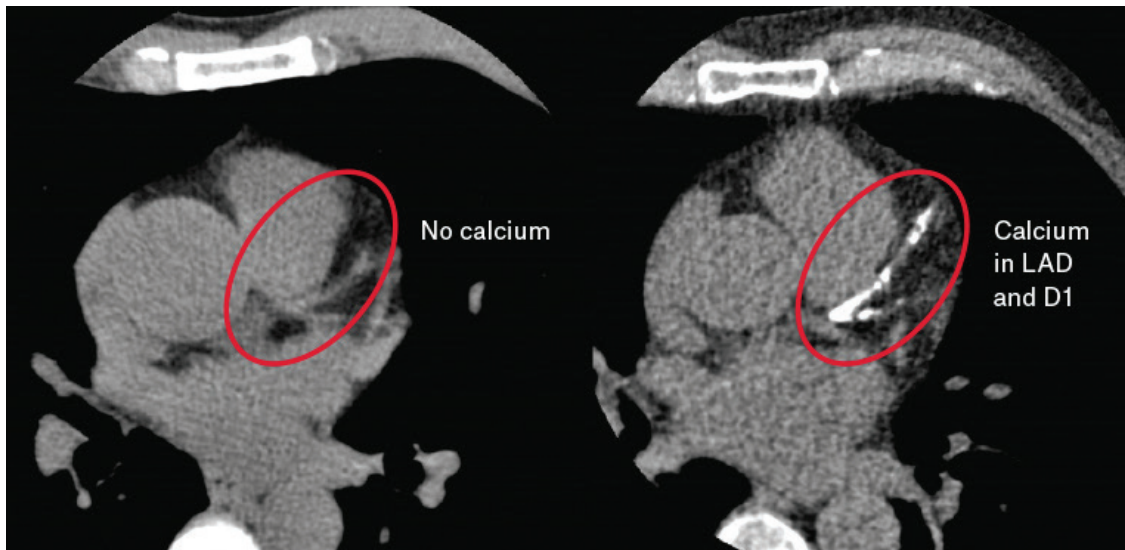


*Robot-assisted surgery for kidney removal*

# CT Coronary Artery Calcium Scoring; Early Prevention of Heart Attacks

**Mr Shifas**

Imaging Technologist, Welcare Hospital Ernakulam, Kerala



**A**ccording to WHO, cardiovascular diseases (CVD) are the primary cause of increasing deaths world-wide. Figures show that a quarter of patients who experience a heart attack display no clinical manifestations. The CT Coronary Calcium score is a simple screening test that calculates the amount of calcium in your heart arteries. More calcium equals more coronary artery disease.

**What are some common uses of the procedure?**

The goal of cardiac CT scan for calcium scoring is to determine if CAD is present and to what extent, even if there are no symptoms. It is a screening study that may be recommended by a physician for patients with risk factors for CAD but no clinical symptoms.

**The major risk factors for CAD are:**

- high blood cholesterol levels
- family history of heart attacks
- diabetes
- high blood pressure
- cigarette smoking
- overweight or obese

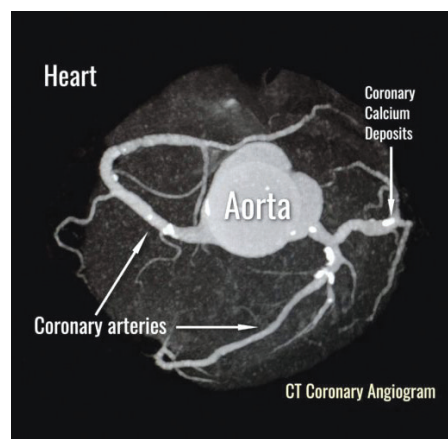
- physical inactivity

**CT coronary ca scoring technique:**

It is a non-invasive, low time consuming, painless, and does not require contrast injection.

**Minimal technical requirement**

- 64-slice scanner
- detector element width  $\leq 0.625$  mm
- option of cardiac CT and ECG-gated triggering



## Preparation

No need of any special preparation, avoid caffeine and smoking for 4 hours prior to the exam.

Sublingual nitrates will be given 15-30 mins before the scan to reduce heart rate.

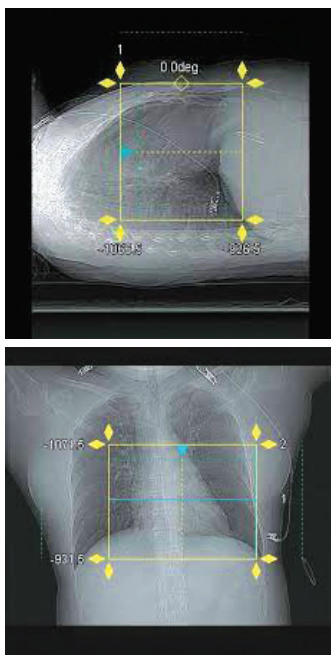
### Position

Supine with arms above the head

ECG leads connected accordance with the manufacturer's guidelines

### Coverage

- just below tracheal bifurcation to below the heart



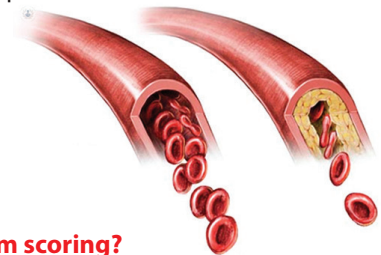
score based on the extent of coronary artery calcification detected by an unenhanced low-dose CT scan

## Method of calculation

The calculation is based on the weighted density score given to the highest attenuation value (HU) multiplied by the area of the calcification speck.

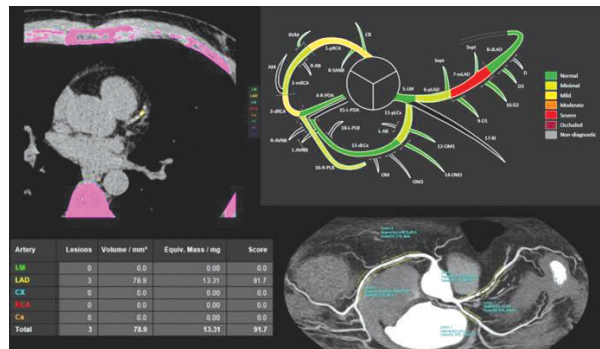
### Density factor

- 130-199 HU: 1
- 200-299 HU: 2
- 300-399 HU: 3
- 400+ HU: 4



### How accurate is Calcium scoring?

Calcium scoring have high level of accuracy towards the calcium plaques, but all the coronary plaques are not calcium plaques, they are limited to calcium scoring. So symptomatic patient with negative Calcium score may need to go for further testing. It is useful for screening purpose.



It CTCS help to visualize lung field surrounded with heart helpful for detect any lung pathology, limited to the region of interest.

Negative result/ less score may need to go for further imaging after a period of time normally 4-5 years gap.

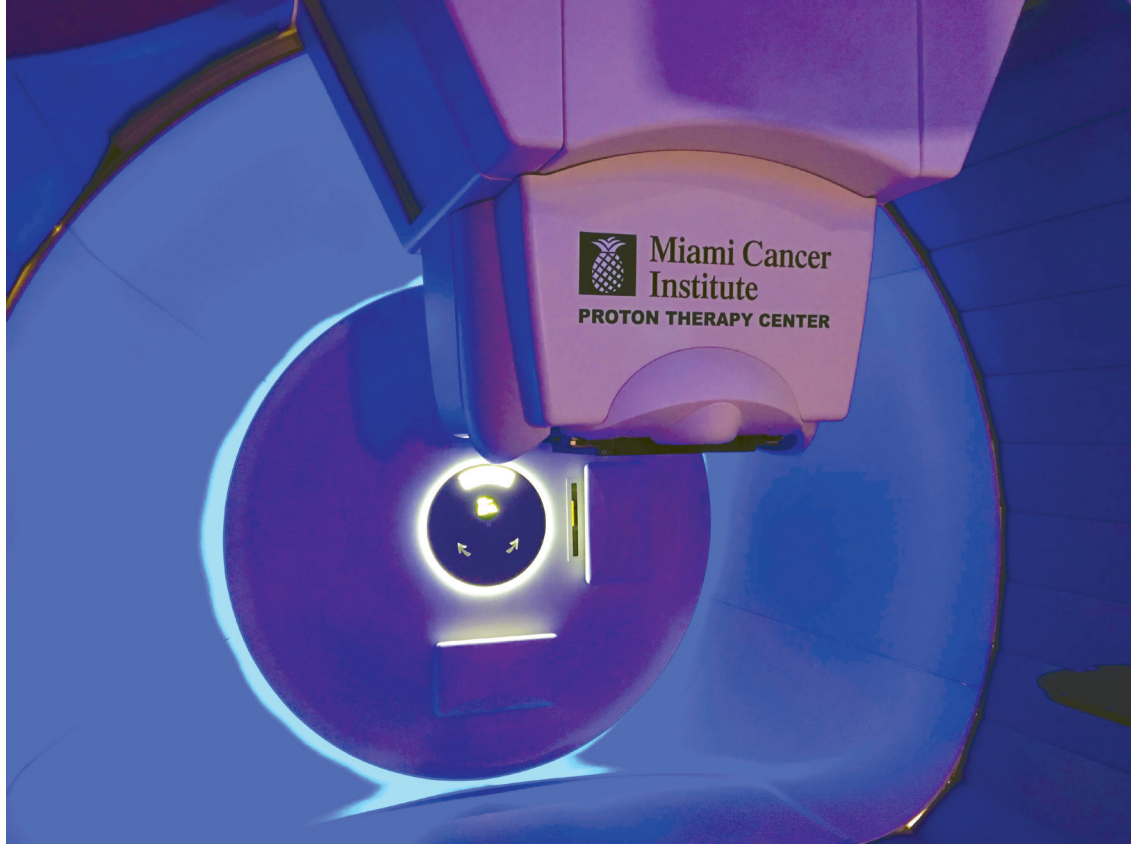
Its useful for screening age above 45 years have high risk of getting cardiac plaques.

### Agatston score:

Agatston score is used to calculate a

### Grading of CAD:

Calcium score	Amount of plaque	Risk level	Treatment
0 None	Low	No treatment	
1-10	Minimal	Low	Lifestyle change/Medication
11-100	Mild	Moderate	Medication
101-400	Moderate	Moderate to high	Medication and further testing if clinically indicated
>400	extensive	high	CAG/ FURTHER testing



# Pencil Beam Proton Therapy says it can meet the target alone!

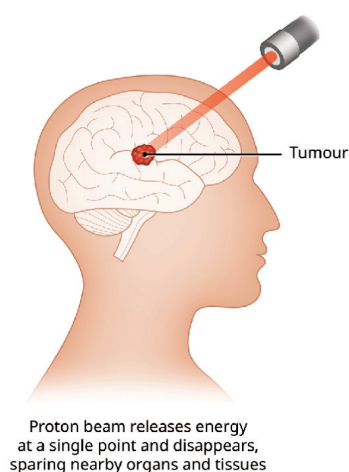
Courtesy- [www.floridaproton.org](http://www.floridaproton.org)

**P**encil Beam Proton Therapy, also called pencil beam radiation, is an advanced proton therapy delivery technique with pinpoint precision. Pencil-beam scanning, also known as spot-scanning, is an advanced form of proton therapy that delivers ultra-fine, targeted doses of radiation to each layer of a patient's tumour. This precision makes pencil beam proton therapy ideal for treating complex cancers. Pencil beam scanning uses magnets to steer the proton beam, creating a customized, three-dimensional delivery shape. During treatment, radiation is deposited layer by layer, conforming the dose to the specific shape of your tumour and destroying cancer cells while preserving critical structures nearby. It's used to treat head and neck, gynaecologic, lung, prostate, breast, brain, liver, lymphoma, sarcoma and tumours in children. Proton therapy may also be used for tumours that recur in areas that have previously been treated with standard radiation therapy.

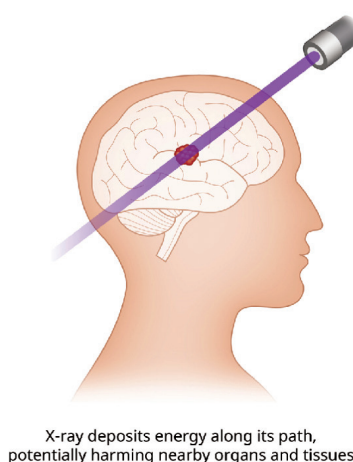
Pencil beam scanning uses a tumour's location, shape and size to create a customized pattern of protons to precisely treat the tumour while avoiding nearby healthy tissue. With standard radiation therapy, energized particles called photons are used to destroy cancer cells. But surrounding normal tissues are also exposed



## Proton Beam Therapy



## Radiotherapy



to the radiation, increasing the risk of side effects. By using a different type of energy called protons, proton therapy is able to treat the tumour while minimizing radiation exposure to the rest of the body. Pencil beam scanning allows for the manipulation of the beam to create a pattern of protons to more accurately administer the dose to the unique shape of the tumour. Pencil beam scanning can treat a tumour with a single field or with multiple fields, sometimes up to five. When multiple scanning beam fields are used, it's called intensity modulated proton therapy (IMPT). When compared to traditional proton therapy, pencil-beam scanning provides greater precision in treating patients, which we couldn't accomplish prior to 2008. Additionally, this form of treatment is a prerequisite for Intensity Modulated Proton Therapy (IMPT). IMPT is another highly specialized form of proton therapy that delivers a precise dose of radiation to tumours in tight spaces, or sensitive areas of the body, through a com-

bination of pencil-beam scanning and other therapies – depending on the patient's individual cancer type. This form of proton therapy is non-invasive and performed as outpatient – allowing cancer patients to maintain their quality of life during and after treatment. Patients undergoing pencil-beam scanning may also receive other concurrent or sequential therapies, such as chemotherapy and/or surgery. This form of proton therapy treats tumours in sensitive areas where conventional radiation therapy may not be the best option. While every patient varies, common benefits include reduced amounts of radiation exposure to surrounding healthy organs and tissue, thus, reducing the risk of acute and long-term side effects such as fatigue, nausea, headaches, breathing difficulties, and dry mouth.

Proton therapy delivers targeted radiation to tumours, guided by some of the world's most accurate imaging technology located onsite at the proton cancer treatment centre. A 220-ton cyclotron is the centrepiece of this proton beam equipment. This machine accelerates protons extracted from hydrogen atoms. It then creates a proton

beam line traveling nearly half the length of a football field at almost the speed of light — with submillimetre accuracy. The protons delivered to the tumour destroy cancerous cells, while minimizing damage to the surrounding healthy tissue. Treatment sessions typically last for 15-40 minutes, with the complete course of treatment lasting an average of six weeks. ●



# SIGNA PET/ MR AIR



## **Shubham Gupta**

Assistant Professor, Faculty of Medicine, Parul University Vadodara, Gujarat

## **Mamta Verma**

Assistant Professor, Department of Radiological Imaging Techniques, COPS, Moradabad, U.P.

**G**E HealthCare is poised to introduce the SIGNA PET/MR AIR during the Society of Nuclear Medicine and Molecular Imaging (SNMMI) 2023 annual meeting. The unveiling will highlight the incorporation of advanced AIR technologies into the SIGNA PET/MR AIR system, aiming to improve diagnostic accuracy, streamline treatment assessment, and enhance overall patient comfort. The recent FDA approvals of novel PET radiotracers and therapeutic methodologies for prevalent diseases like prostate cancer and Alzheimer's Disease underscore the demand for dependable and holistic imaging solutions across the entire patient care continuum. The SIGNA PET/MR AIR integrates GE Health Care's distinctive AIR technologies to meet the changing needs of diverse patient populations. These cutting-edge technologies comprise AIR Coils, enhancing patient comfort, AIR Recon DL, improving MR image quality and reducing scan time, and Motion Free Brain, mitigating motion-related PET image degradation.

The recent endorsement of drugs exhibiting disease-modifying potential necessitates additional imaging of patients using both MR and PET. The SIGNA PET/MR AIR introduces the industry's most sensitive Time-of-Flight (ToF) PET detector in a PET/MR configuration, allowing clinicians to attain the earliest possible diagnosis, gain insights into disease progression, and identify adverse effects in a single scan. Addressing the issue of patient movement during imaging examinations, the Motion Free Brain PET represents a groundbreaking solution on SIGNA PET/MR AIR, effectively managing motion without relying on external tracking devices. This innovation ensures consistent image quality, even in challenging patients, potentially leading to quicker and more accurate diagnoses while minimizing the likelihood of repeat scans.

The Signa PET/MR air system upholds our tradition of introducing cutting-edge technologies aimed at addressing a broad spectrum of clinical diseases," stated Jie Xue, President and CEO of MR at GE HealthCare. Our latest PET/MR technology is poised to directly impact the most formidable diseases, such as prostate cancer and Alzheimer's Disease. These conditions necessitate precise and comprehen-

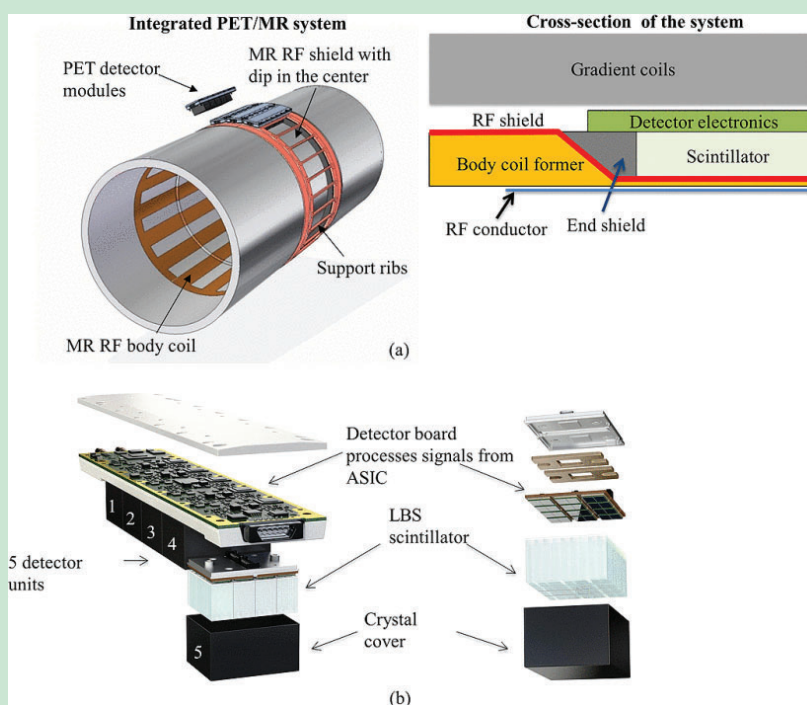
sive imaging to ensure accurate diagnosis, treatment planning, and therapy monitoring. Witnessing Signa PET/MR air tackling these challenges is thrilling, aligning with our vision of delivering advanced, personalized care.

The integration of MR and PET imaging modalities into a simultaneous hybrid system holds promise for assessing biochemical processes in tissue, supplemented by anatomical information with excellent soft-tissue contrast. Using MR instead of CT as the anatomical complement to PET can result in reduced patient radiation dose and improved soft tissue contrast. The simultaneous acquisition of PET and MR data presents opportunities for studying processes with excellent spatial and temporal correlation between modalities. Additionally, the use of various MR pulse sequences allows for greater tissue differentiation. However, integrating PET and MRI into a single system capable of simultaneous operation poses challenges. For true simultaneous imaging, both PET and MR components must acquire data from the same imaging volume, eliminating the option to physically offset one system relative to the other, as seen in PET/CT. This limitation imposes design constraints such as space limitations, vibration issues, variable thermal load, and susceptibility to electromagnetic interference.

Operating a vacuum photomultiplier (PMT) in strong magnetic fields, common in MR imaging, is not feasible. The solution involves either relocating the PMT to a region with a weaker magnetic field or substituting it with a different photosensor. Avalanche photodiodes (APDs) and, more

recently, silicon photomultipliers (SiPMs), have enabled the development of PET detector designs with a small footprint capable of functioning in strong magnetic fields.

A hybrid brain PET/MR system based on APDs was developed for neurodegenerative applications. Commercially introduced clinical PET/MR scanners include an APD-based non-time-of-flight (nonTOF) integrated system and a PMT-based TOF sequential system. A trimodality system (TOF-PET/CT and MR) with a dedicated shuttle has also been introduced for sequential PET/MR imaging. Time-of-flight (TOF) PET technology, particularly



(a) Schematic of the PET/MRI integrated system, showing the cross section of a detector integrated with the RF body coil; (b) Schematic of a detector mobile and unit.

advancements in TOF PET detectors, enhances PET image quality, especially in larger patients. Recent progress in TOF PET detectors is attributed to fast, bright scintillators coupled with high-gain, magnetic-insensitive photosensors, with silicon photomultipliers (SiPMs) proving suitable for TOF detectors due to their high gain, low noise, and



magnetic insensitivity.

This work details the design and technical performance evaluation of a TOF-capable SiPM-based clinical PET detector integrated with a 3T MR scanner. The assessment includes the impact of the PET detector ring on the MR system's performance and vice versa, along with an evaluation of the radiofrequency (RF) body coil's performance. A comprehensive NEMA PET performance characterization and clinical evaluation are conducted separately.

### Discussion

This innovative scanner incorporates a unique RF body coil, specifically crafted to integrate a PET ring seamlessly without sacrificing the quality of MR images. The experiments detailed in this paper were conducted using a prototype system that mirrors the design and functionality of the commercially accessible SIGNA PET/MR. Notably, this system introduces a groundbreaking use of Analog SiPM-based PET detectors in a clinical whole-body setup for the first time. This integration delivers PET images of exceptional resolution, complemented by Time-of-Flight (TOF) capability, even within the challenging magnetic resonance (MR) environment.

### Conclusion

In essence, the GE SIGNA PET/MR system,

equipped with Time-of-Flight (TOF) capability, holds significant potential to deliver imaging results that are either comparable to or surpass those achieved when using distinct PET and MR systems. The anticipated outcome is an enhanced imaging performance, particularly in intricate clinical scenarios. Ongoing efforts will focus on investigating its applications in functional Magnetic Resonance Imaging (fMRI)/Positron Emission Tomography (PET) techniques.

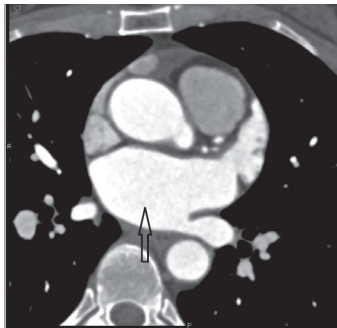
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Compiled by : **Prasad P P**

1. What is the K -absorption edge of Barium containing contrast media?
2. Which area of the brain is associated with speech?
3. In CTV and PTV in radiotherapy, C and P stand for?
4. What is the medical term for bleeding from the nose?
5. What venous device is preferred for a patient requiring IV injections at frequent or regular intervals?
6. The most proximal portion of the pharynx is?
7. To which modality K space is associated with?
8. Dual energy CT is also known as?
9. In radiotherapy the wall of the passage from the console room to the treatment room is usually referred as?
10. The quantitative assessment of the radiotracer uptake from a static PET image is referred as?
11. The pain experienced by an individual whose coronary arteries are not conveying sufficient blood to the heart is called?
12. In pediatric imaging a child from birth to 28days is termed as?
13. The movement of a part towards the midline of the body is termed as?
14. The radiological examination for the demonstration of uterine and tubal patency is known as?
15. Identify the chamber of the heart?



Please mail your answers and contact number to [alaraquiz@isrt.org](mailto:alaraquiz@isrt.org) in before **15<sup>th</sup> February 2024**, The subject of mail should be given as **ALARA Q-92**

## Answer Key Q-91

- |                          |                            |
|--------------------------|----------------------------|
| 1. 220 Hz                | 9. Dr.Raymond Wahan        |
| 2. 33.2 KeV              | Damadian                   |
| 3. Shoulder joint        | 10. Erythema               |
| 4. Occipital lobe        | 11. Knee joint             |
| 5. Aluminium oxide       | 12. Ampoule                |
| 6. Monteggia fracture    | 13. Left lateral decubitus |
| 7. Wernicke's area       | 14. Dyspepsia              |
| 8. Photo electric effect | 15. T2 weighted            |

**Winner : Rakesh Poojari**, Indore, Madhya Pradesh



## George Doring Ludwig

**B**orn in Johnstown, Pennsylvania in 1922. He received his Bachelor of Science degree in Chemistry from the St. Vincent College, Latrobe in 1944 and his medical degree from the University of Pennsylvania in 1946. After his graduation, and between 1947 and 1949, Ludwig was on active duty as junior Lieutenant at the Naval Medical Research Institute in Bethesda, Maryland. There, with an inquisitive mind, and upon the suggestion from surgical colleague Charles Kirby at the University of Pennsylvania that ultrasonics might be developed into a technique for the detection of gallstones, he began experiments on animal tissues using A-mode industrial flaw-detector equipment (initially with the Sperry reflectoscope). Ludwig designed experiments to detect the presence and position of foreign bodies in animal tissues and in particular to localise gallstones, using reflective pulse-echo ultrasound methodology similar to that of the radar and sonar in the detection of foreign boats and flying objects.



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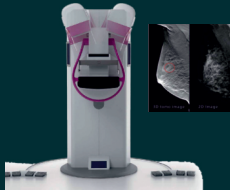
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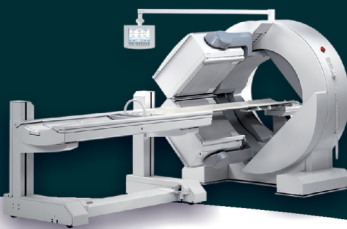
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Sequoia Healthcare Pvt. Ltd. Plot No.27, Survey No.125, KIADB Industrial Area,  
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Building No.1, District No.7, URANUS Avenue, AMTZ Campus, Near Pragati Maidan, VM Steel Projects, S.O Visakhapatnam - 530031