

# **Portable Quantum Sensor for Early Cancer Detection**

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## Abstract

Portable devices that possess the remarkable capability to perform accurate, fast, and ultra-sensitive detection of early-stage cancer are not only profoundly desirable but also critically important to assist the decision-making process within the field of oncology. Their ultimate objective is to significantly improve outcomes associated with primary therapies. In this context, we are absolutely thrilled to report the groundbreaking design and development of an innovative and highly portable quantum sensor that has been specifically engineered for early cancer detection. This remarkable sensor relies on a stunning new generation of advanced quantum sensors that cleverly harness unique quantum mechanical effects to achieve its goals in cancer detection. The application of these extraordinary quantum phenomena to the crucial area of pollutant sensing allows for substantial enhancements across various critical parameters such as sensitivity, accuracy, and detection limits, which are essential to the successful identification of disease markers. These significant advancements enable the precise sensing of vital biomolecules that are typically present in extremely low concentrations, which is itself paramount in the early detection of important cancer markers. The portable sensor detailed in this report meticulously implements these cutting-edge concepts and is currently undergoing rigorous development as we transition it from the initial proof-of-concept stage to an exciting first pre-commercial prototype phase. This state-of-the-art

device is equipped with specialized readout electronics that can be seamlessly integrated with sophisticated FPGA and microcontroller units, thereby enhancing its overall functionality and operational capabilities, which are crucial for effective cancer detection. Furthermore, this innovative device is designed to include an electro-chemical cell, providing users with a user-friendly Python-PC interface that facilitates streamlined interaction and comprehensive data analysis, both of which are indispensable for medical professionals. This pioneering sensor empowers users by enabling a thorough and detailed analysis of the solution under test, skillfully leveraging its innovative and cutting-edge design. Given the device's remarkable portability, combined with its ultra-high sensitivity, it is exceptionally well positioned to detect molecular signatures that may indicate the early stages of cancer. This exceptional capability offers significant and timely support for improved oncology diagnosis and fundamentally enhances patient outcomes, making it an undeniably transformative and revolutionary tool in the ever-evolving realm of cancer detection and treatment.

# Chapter - 1

## Introduction to Quantum Sensing

Quantum sensing exploits quantum correlations in microscopic systems, registering extremely subtle changes that classical counterparts cannot resolve. In quantum mechanics, microscopic systems have only discrete stationary energy levels. Reduction or decoherence of superposition states by the environment converts a quantum system into a classical mixture, accompanied by information leakage. The effect of an environment on a quantum system can also be studied classically, investigating changes in classical trajectories of a disturbed probe. However, the probing range is limited by technological constraints: it is impossible to access subatomic length scales, and back action inevitably modifies the environment <sup>[1]</sup>.

Quantum sensors overcome these constraints by exploiting a quantum interaction. Superposition states allow a quantum system to have several configurations “simultaneously”. An environment that influences a quantum system changes the phase difference between the components of the superposition state. Complementarity guarantees that the information stored in the phase of a quantum system is inaccessible to a classical environment, protecting the quantum sensor. Moreover, the information

about environment perturbation is encoded as local phases on the superposition state components. Quantum systems can influence each other at arbitrary distances by “transferring” their local phases, carrying information to remote locations, where it can be read out by a measurement.

Recent advances in the field of quantum-enhanced sensing have uncovered significant value for a diverse array of applications. These applications include, but are not limited to, refinements in imaging and microscopy, precise detection of elusive dark matter and gravitational waves, as well as robust testing of foundational physical models. The ongoing developments in the miniaturization of atomic-scale sensing devices have greatly enabled the execution of highly sensitive measurements on various cellular specimens. This breakthrough is unlocking tremendous potential, paving the way to revolutionize both the physical sciences and life sciences in ways that were previously unimaginable. With these advancements, researchers are now able to explore intricate details and complexities that may lead to groundbreaking discoveries [2, 3, 4, 5, 6].

## **1.1 Overview of Quantum Mechanics**

Quantum sensing exploits quantum mechanical effects to measure physical quantities with exceptionally high precision, surpassing classical sensor capabilities. Advances in quantum control and fabrication have prompted the development of applications such as clocks, magnetometers, accelerometers, and imaging systems. Motivated by the need for enhanced control and sensing of diverse physical fields, and leveraging atomic, optical, condensed matter,



and nanoscale platforms, quantum sensing addresses the limitations of classical methods [7].

Quantum mechanics, as a foundational framework within the field of physics, imposes fundamental and intrinsic limits on how easily one can manipulate, process, and transmit information within quantum systems. These critical limits serve to delineate and define the efficiency and capabilities of both natural systems and engineered processing devices. Despite the existence of these constraints, it remains entirely possible to utilize the inherently quantum elements present in nature to construct innovative devices that demonstrate enhanced operational efficiency. Significant and ongoing research efforts are actively focused on identifying, characterizing, and exploiting such quantum elements across various domains of application, including but not limited to sensing, advanced computation, secure communications, and cryptography, all of which benefit from the unique properties of quantum mechanics [8, 9, 10, 11, 12].

## **1.2 Principles of Quantum Sensing**

Quantum mechanics describes a physical system of conserved energy  $E$  according to an equation introduced in 1927 by Erwin Schrödinger. Measurements of an observable quantity several times on the same quantum system will yield a number of values with a standard deviation of at the least the order of magnitude of the observable's quantum fluctuations. Controlling the state of a single physical system and measuring this state provides a radically enhanced level of sensitivity to any external perturbation. Such a quantum system may function as an ultrasensitive sensor.

Quantum sensing is a field that involves the application of a quantum system, leveraging quantum properties or utilizing quantum phenomena to perform precise measurements of various physical quantities. The physical quantity being measured is generally linked to a Hamiltonian term that is integrated into the overall total Hamiltonian of the quantum system under observation. This innovative approach of quantum sensing enables scientists and researchers to achieve measurement sensitivities that are impossible to reach using classical methodologies. Additionally, it allows for the provision of spatial or temporal resolutions that are otherwise unattainable and facilitates the exploration of entirely new types of measurements that can yield valuable insights. It is essential to note that the broad concept of quantum sensing does not confine itself to any specific measurement strategy or technique. On the other hand, more focused definitions of quantum sensing closely associate the term with metrological practices that rely on non-classical states of the sensing system, thus highlighting the progressive impact of quantum mechanics on measurement science [9, 11, 10, 13].

# Chapter - 2

## Cancer Detection Technologies

Cancer detection encompasses a variety of techniques aimed at the early-stage identification, accurate diagnostics, and thorough monitoring of cancer. The importance of early detection cannot be overstated, as it enables timely medical intervention, which significantly mitigates cancer's aggressive progression and improves patient outcomes, leading to higher survivability rates. Current methods employed for cancer detection often rely heavily on various clinical imaging techniques such as ultrasound and computed tomography, in addition to biochemical analyses that can provide crucial information. Furthermore, electroanalysis platforms are emerging as advantageous tools that offer low-cost solutions and the adaptability required for point-of-care formats, which can be particularly beneficial in resource-limited settings. The development of advanced electrochemical sensors that specifically target circulating tumor cells, nucleic acids, exosomes, proteins, and metabolites has gained significant attention in recent years. These innovative sensors incorporate nanostructured materials—such as graphene, carbon nanotubes, and metal nanoparticles—that serve either as supporting electrodes or as interface coatings. These materials are instrumental in preserving the activity and stability of biorecognition components through enhanced electron transfer and

increased surface area, which are critical for effective detection. Established clinical protocols, including low-dose computed tomography (CT), bronchoscopy, and histopathology, continue to play vital roles in cancer diagnosis. However, these methods are often resource-intensive, poorly standardized, and fail to support multiplexing capabilities, which can limit their effectiveness in various clinical scenarios. On the other hand, industrial electronics are being increasingly explored for the development of portable biosensors and point-of-care diagnostics. This includes advancements in micro-electromechanical systems and integrated photonics. Despite these innovations, challenges remain, particularly concerning restrictive sensitivity levels and a continued focus on a limited range of bio-agent categories. In this dynamic context, quantum technologies are progressively being considered as a potentially disruptive approach that could not only address existing limitations in cancer detection but also open up exciting new applications that could vastly improve the landscape of cancer diagnostics and monitoring in the future [14, 15, 16, 17, 18, 19].

## **2.1 Current Methods in Cancer Detection**

The selection and optimization of detection techniques aimed at identifying minute biological quantities represent key challenges that must be addressed in order to provide patient-specific information that is essential for effective medical care. This is particularly relevant in the context of methods designed for early cancer diagnosis and therapy guidance. The early detection of cancer is not only crucial for implementing effective treatment strategies but also

plays a significant role in achieving a higher survival rate among patients diagnosed with this serious disease. Tumor markers, also referred to as cancer biomarkers—specific biological molecules that are overexpressed or produced by cancerous tissues—can serve as valuable indicators that assist in the early diagnosis of cancer. Furthermore, real-time monitoring of intracellular signaling pathways has the potential to provide early warnings of cancer formation, and this can occur potentially even before the appearance of any physical symptoms that typically prompt further evaluation. The range of detection techniques available spans various methods, including direct blood sample analysis, where the concentrations of tumor markers are measured, and advanced imaging methods such as ultrasound, magnetic resonance imaging (MRI), and X-rays. It is important to note that many of these imaging techniques, while useful, necessitate potentially harmful irradiation and often exhibit limited reliability; elevated tumor marker concentrations may indicate a general disease state rather than pointing to a specific type of cancer. Accordingly, the median age of cancer diagnosis is approximately 66 years, which underscores the pressing need for early-detection technologies that are suitable for individuals across all age groups. These considerations highlight the ongoing challenges in the cancer detection landscape and the critical importance of further advancing diagnostic methodologies to improve outcomes for patients of various demographics [20, 21, 22, 23].

Cancer emerges from uncontrolled cell growth and is among the leading causes of death globally <sup>[1]</sup>. More than

100 types of cancer have been recognized, each named after the organ or tissue of origin. Detecting cancer at the earliest stages remains the cornerstone of effective therapy and enhanced survival rates. Although biopsy prevails as the definitive diagnostic procedure, it is invasive, time-consuming, and accompanied by potential discomfort and secondary complications. Consequently, research efforts now emphasize the design of rapid and non-invasive detection modalities based on biosensors for cancer biomarkers present in blood and other bodily fluids. Such platforms promise prompt preliminary screening, thereby facilitating the timely administration of confirmatory tests and consequent initiation of appropriate therapeutic protocols.

### **Traditional Imaging Techniques**

Non-invasive imaging techniques have played a crucial role in cancer detection by providing detailed visualization of anatomical features and internal tissue changes. Plain X-rays are the most widely used and convenient imaging modalities, capable of providing critical information about bone structures and the detection of calcifications and abnormal masses in soft tissues. Computed Tomography (CT) allows for the assessment of two- and three-dimensional visualization of the body, differentiating structures based on varying attenuation densities. Magnetic Resonance Imaging (MRI) offers superior soft-tissue contrast, delivering highly detailed anatomical images for diagnosis and characterization of lesions. Ultrasound imaging, based on the speed of sound through various tissue layers, permits instantaneous real-time imaging and

functional assessment through Doppler techniques <sup>[2]</sup>. While these technologies are invaluable for large tumors, the use of ionizing radiation in X-ray-based modalities such as plain X-ray, CT, and Positron Emission Tomography (PET) raises concerns about radiation exposure. Although molecular diagnostic techniques provide enhanced precision for detecting minimal residual disease and non-invasively assessing treatment response, their widespread adoption is hindered by inter-individual variations, validation challenges, and significant costs <sup>[3]</sup>.

X-rays are a form of electromagnetic radiation discovered by Wilhelm Röntgen in 1895. Medical applications quickly followed, utilizing X-ray imaging for clinical diagnosis. X-ray imaging systems generate a collimated beam of X-rays that passes through biological tissue and strikes a radiation sensor placed behind the patient <sup>[3]</sup>. Different tissue compositions attenuate the beam to varying degrees. Dense tissues such as bone strongly absorb X-rays, while soft tissues absorb less. Lesions and tumors attenuate the beam differently from surrounding tissue, thereby producing contrast in X-ray images. Early X-ray imaging devices relied on photographic film for image acquisition, but modern systems use digital radiography. Digital X-ray imaging utilizes computed tomography (CT) image processing software to reconstruct three-dimensional image volumes from numerous two-dimensional images. The resulting images improve tissue contrast and enable detailed examination from any angle. Since its discovery, X-rays have remained a critical diagnostic tool due to their ability to provide non-destructive internal visualizations of

the human body. X-ray imaging is a cost-effective, widely available, and rapid screening technique. It is frequently employed by physicians for cancer diagnosis and treatment planning.

Computed tomography (CT) plays a pivotal role in the detection, characterization, and staging of lung cancer and other thoracic malignancies <sup>[4]</sup>. Since the introduction of clinically viable dual-energy CT techniques, substantial evidence has accumulated on its use for imaging chest malignancies. The technology provides high-resolution anatomic imaging, which remains central to imaging efforts despite the availability of other modalities. Dual-energy CT enhances the detection and staging of thoracic cancers by permitting visualization of lesion enhancement associated with angiogenesis and other markers of disease activity. Light-emitting diode (LED)-based CT systems, using energy integrating detectors (EIDs) in the clinical setting, have demonstrated encouraging results in preclinical imaging. Preliminary investigations reveal that LED-based CT systems are capable of imaging 3-D structures in small animals doped with iodine-based contrast agent.

Magnetic Resonance Imaging (MRI) offers a non-invasive approach to cancer detection, employing radio waves to excite hydrogen atoms in a high-field magnet, whose longitudinal and transverse magnetizations are then read out by the receiver coils of the scanner. Contrasted with X-ray modalities, MRI detects disparate tissue properties; the ontological form of image contrast derives from the sensitivity of protons to both intrinsic tissue properties such as proton density, and extrinsic experimental parameters



such as repetition time (TR), echo time (TE), and the amplitude and timing of field gradients. High-resolution images of soft tissue then permit the identification of tumors or metastases by their altered intensities in angiographic examinations, as well as in diffusion- and susceptibility-weighted imaging.

Although a wide variety of MRI-based techniques now target many forms of cancer, breast cancer—expected to affect 276,480 females and cause 42,170 deaths in 2020—serves as a useful paradigm for describing the current state of the art. Indeed, up to 12% of the 12.4 million mammography screenings performed annually in the United States lead to misdiagnosis, underscoring the need for alternative or complementary modalities. Mammography is complemented by MRI, whose cancer-screening sensitivity is higher and was recently measured at 93% for high-grade tumors as small as 8 mm. The primary stage of investigation now seeks to improve specificity, which fluctuates between 37% and 97% and reflects the challenge of distinguishing malignant from benign lesions. Data further indicate that false-positive rates differ between high-risk and low-risk lesions, thereby encoding biological differences with prognostic implications. Secondary issues addressed include the emergence of male breast cancer, whose incidence is three orders of magnitude lower than its female counterpart; MRI detection, which is gaining increasing attention; worsening survival trends; and treatment protocols frequently derived from female cohorts. Progress in MRI and MR spectroscopy has meanwhile enhanced the identification of breast-cancer biomarkers and facilitated

measurements of treatment response, whose variation correlates with tumor characteristics such as hormone-receptor expression and malignancy [5].

Ultrasound is an inexpensive, fast and non-invasive diagnostic imaging technique commonly used for cancer detection [6]. Compared to X-ray and CT scans that are based on ionizing radiation, the echoes produced by sound waves can be converted into an electronic format that is much easier to analyze [7]. One area of interest is prostate cancer since ultrasound images from transrectal probes can detect abnormalities such as tumors or calcifications. Due to the difference in neovascularization, prostate cancer can be identified because the tumoral tissue's blood supply is not coupled to the glandular epithelium, which changes the ultrasound absorption. As a result, the cancerous tissue's echoes have a statistical behaviour that is distinct from its surrounding tissues and can be identified by an algorithm that uses a statistical model in conjunction with a Markov random field and morphological operators to incorporate spatial information. Classification errors remain a fundamental problem due to the inherent difficulty of the prostate cancer diagnosis task. Radiologists may be fooled by pathologists. Computer-aided diagnosis systems have mainly concentrated on the visual characteristics of the grey-level image from the original B-mode ultrasound, although information from additional modalities are often available and further analysis techniques exist.

One possible approach to prostate cancer detection consists in the use of texture analysis. With the development of artificial intelligence, machine learning techniques have

found various applications in medical image analysis. After having been trained on a number of cases, a classifier, with algorithms such as support vector machines, decision trees or random forests, is able to categorize new, unknown images or sub-regions of images. In this context, features extracted from the medical images, like texture, shape or a combination thereof, can be used as input to characterize the input data. Applications concern liver, thyroid or bladder cancers that are often examined with ultrasound imaging. In the case of prostate cancer, only a few studies address the problem of computer-aided detection. A prominent example is a semi-automated system where user-chosen regions of interest are classified according to features extracted from the transrectal ultrasound images. The system achieves reasonable results with a sensitivity and specificity of both above 80 % [8]. Such encouraging outcomes suggest that texture analysis may be useful in cancer detection. Similarly, a study on microtexture information displayed that distinguishing cancer from non-cancer tissues is possible within certain limits. Texture features in general take into account not only the distribution of pixel intensities but also the relationship between adjacent pixels. This information deals with the degree of heterogeneity reflected by images and enables the nature of lesions to be established as demonstrated in previous studies where the prediction of malignant renal tumours or colorectal cancers exhibited a high diagnosis accuracy.

Cancer detection offers medical practitioners a means to detect specific types of cancer in high-risk individuals and monitor established cancer during and after therapy. Routine, population-wide screening measures are frequently

employed without regard to individual risk. For instance, in the United States, all persons aged 50-74 years are recommended to undergo routine screening for colon and lung with computed tomography (CT) and endoscopy. Over age 21, cervical cancer screening is offered, followed by routine mammography and prostate specific antigen (PSA) after 40 and 50 years of age, respectively. Cancer detection also permits early diagnosis of symptomatic secondary tumors, and finally, it can be exploited to advance chemoprevention and chemobiological intervention of primary cancer <sup>[9]</sup>.

Recent advances in molecular diagnostics complement genetic and histological data, providing robust means for diagnosis, prognosis, or prediction of patient response. Molecular bioassays detect individual or multiple biomarkers, present in tumor tissues or bodily fluids, with confirmed specificity for particular cancers. Marker association with specific parameters and prognosis makes this approach the main tool for cancer analysis, from basic research to clinical practice <sup>[10]</sup>.

Molecular diagnostics for breast cancer are constructed to determine the presence and extent of cancer, predict the likelihood of response to pre-surgical and systemic therapy, and monitor recurrent disease. Derivation of the underlying molecular bioassay involves also defining the etiological type of breast cancer, considering heterogeneity among breast cancer groups, and linking etiological types to clinical manifestations, histology, growth rate, genetics, and specific molecular markers; the test should be externally validated and reproduced.

The identification of clinically relevant biomarkers constitutes a crucial first step towards enhancing cancer detection capabilities. Various methodologies have been established to facilitate tumor specimen preparation that retains nucleic acids, proteins, and structures with in situ localizations, thereby enabling multiplexed quantitative evaluations using antibodies, RNA-binding proteins, or nucleic acid probes. These approaches illuminate critical hallmarks associated with carcinogenesis and tumor progression. Emerging biosensor platforms harness multiple biotransduction principles—including optical detection (fluorescence, surface plasmon resonance, surface-enhanced Raman scattering), ECG-derived signals, mechanical resonance, and electrochemical alterations—to identify potential cancer biomarkers <sup>[11]</sup>. The extensive characterization of the human proteome continues to yield candidate molecules across diverse tumor microenvironments; characterizing these biomarkers in serum or plasma offers the prospect of non-invasive, cost-effective diagnostic assays suitable for widespread population screening. Despite substantial investment, few biomarkers have transitioned into clinical practice due to defective validation studies, often reliant on convenience samples, pre-surgical specimen collection, and inadequate statistical power during validation, which overlook critical factors such as genetic variability, environmental influences, and tumor size <sup>[12]</sup>. Consequently, there is a growing imperative for human studies that generate informative sample banks and facilitate robust independent validation of candidate panels. Well-characterized cancers display a host of functional alterations in cell surfaces and

interactions, manifested as changes in antigen expression and receptor engagement with the extracellular matrix. These molecular perturbations produce signature profiles exploitable for refined diagnosis and prognosis. Non-invasive detection methodologies employing biosensors—devices incorporating a biological sensing element coupled with a transducer—offer rapid, sensitive, selective quantification of relevant analytes while remaining cost-effective and suitable for point-of-care applications. In cancer biosensing, recognition agents include monoclonal antibodies, aptamers, and molecularly imprinted polymers immobilized on sensor surfaces; optical and electrochemical transduction techniques have been favored for their proven sensitivity, enabling detection across a broad dynamic range [1]. Table 3.1 systematically summarizes biomarkers associated with a spectrum of solid tumors, categorized by clinical utility (diagnostic, prognostic, predictive) and molecular class (proteins, nucleic acids), thereby guiding the selection of targets for biomarker and biosensor development.

Genetic testing methods represent a key technological advancement in cancer detection, owing to their potential for precise identification of cancer risk. Early genetic cancer testing focused upon single-gene testing for high-risk genes such as BRCA1 and BRCA2 [13]. The development of next-generation sequencing technology enabled multigene panel testing and made it feasible to test for risk of a wide variety of inherited cancers simultaneously. Such tests have high sensitivity and specificity for pathogenic mutations [14].

Prophylactic measures such as bilateral salpingo-

ophorectomy are effective at reducing risk of cancer for those individuals with inherited mutations. Genetic information also informs targeted and personalized therapy in patients already diagnosed with cancer, and test results provide options for genetic counseling and at-risk family member services. Patients with a family history of cancer or other risk factors can now be tested for pathogenic mutations in 34-36 genes associated with hereditary predisposition to cancer, providing a strong indication for the need for and use of genetic testing <sup>[15]</sup>.

Analysis of circulating tumour DNA could provide another avenue for cancer detection. The presence of aberrantly methylated DNA and mutation analysis can be used to detect early-stage cancer. Tumour exosomes present another liquid biopsy target. Proteomic analysis and tumour-related proteins circulating in plasma or on exosomes enable the potential for pan-cancer advanced screening, probing malignancy of early tumours, minimal residual disease, drug susceptibility, drug resistance, metastatic potential, and disease prognosis. When an entire tumour genome is present in the circulatory system in the form of plasma, exosomes, and circulating tumour cells, with components that cross the blood-brain barrier, numerous cancer-associated signals beyond ctDNA can be leveraged. When coupled with single-molecule, single-cell circulation tumour load-enhancing technology, such techniques represent a powerful approach to cancer detection.

Circulating tumor DNA (ctDNA) analysis represents one of the most exciting advances in cancer detection.

Precancerous and cancerous tumors shed DNA into the bloodstream, and these ctDNA fragments have a characteristic set of mutations, epigenomic features, and patterns of fragmentation in comparison to DNA shed from healthy tissues. Analysis of ctDNA can therefore reveal the presence of a tumor anywhere in the body. Detection of ctDNA in a blood sample is often referred to as liquid biopsy. Noninvasive blood panels for early detection of cancer and assessment of cancer prognosis are currently undergoing clinical trials.

Several companies offer commercial tests for ctDNA analysis. Testing can include assessment of tumor load during treatment, early detection of residual disease after surgery, and pre-symptomatic detection of cancer relapse. There are also tests for early detection of a variety of cancer types in patients without cancer symptoms—e.g., CancerSEEK. These tests are still in development; screening guidelines do not yet recommend them.



# Chapter - 3

## Histopathological Methods

Histopathological, immunohistochemical, and FISH techniques require a tissue biopsy for confirmation after an abnormality has been detected by molecular or imaging methods <sup>[16]</sup>. Histopathological analysis is central to the diagnosis, therapy planning, and follow-up of many cancers. It provides a direct visualization of tissue morphology and cellular structures unfamiliar to genomics and proteomics studies. Pathologists carefully examine tissue to determine its type—normal, inflamed, pre-malignant, malignant, or benign—and use the results of this examination to guide treatment. The standard histopathology approach requires that tissue be processed and fixed, embedded in paraffin wax or frozen, sectioned with a microtome, fixed on a microscope slide, and stained by a pathologist with dyes such as haematoxylin and eosin (H & E) prior to conventional brightfield microscopy. These labor-intensive procedures are a major bottleneck in clinical analysis.

An ideal histology-like method would image tissue morphology directly from preserved specimens without the need for sectioning and staining and interrogate the full suite of tissue types used by pathologists such as FFPE blocks, paraffin-embedded sections, and frozen tissues. Most clinical tissue is archived as FFPE blocks or sections. FFPE

blocks are optically opaque and therefore preclude trans-illumination modalities that typically form the basis of histology-like imaging. Consequently an imaging approach operating in reflection mode is desirable. Sections and blocks fixed in formalin are highly scattering and present challenges for high-resolution imaging at depths of a few millimeters. In addition, the medical community has emphasized the need to visualize cell nuclei clearly because many diagnostic criteria depend on examination of nuclear morphology. Label-free approaches have therefore been developed to reproduce the abundant nuclear contrast seen in conventional histology. Finally, the most widely available preparation method is paraffin embedding and subsequent deparaffinization because of the worldwide adoption of standard operating procedures in histopathology laboratories <sup>[17]</sup>. Recent studies in molecular biology have steadily improved diagnostic molecular pathology and automated systems are widely utilized for analysis of cells in fluids and smears, but the complex mixture of morphologies present in tissue sections precludes such analysis, leaving traditional histology as the most effective method for diagnostic work.

Tissue biopsy techniques, mainly needle- or endoscopy-assisted, enable samples from any accessible organs with minimal invasion. Endoscopic biopsy is routinely employed for cases in the esophagus, stomach, colon, lung, urinary bladder, in conjunction with endoscopic visualization. For cancers in more locations, needle biopsy is conducted with surgical guidance, chiefly imaging guidance <sup>[18]</sup>. In addition to pathological examination, ultrasound and optical imaging

can help intraoperative detection in real time, enhancing diagnosis and intervention. Real-time tissue feature profiling with incorporated dose of chemotherapeutic agent has recently been developed for brain cancer therapy under the guidance of needle biopsy <sup>[19]</sup>.

Immunohistochemistry (IHC) caters to both routine diagnostic workflows and research endeavors and continues to consolidate its position on the cancer detection landscape. IHC emerged as a widely adopted alternative to enzyme-linked immunoassays and radioactive imaging. Radiolabeled antibodies dispersed throughout the body yielded ambiguous results for tissue exploration at single-cell resolution, while IHC permits differential staining of biomarkers when coupled with image processing. Variations in stain intensity provide key information content for scoring—emulated by open source software such as IHC Profiler—which can be repurposed to protein expression, aiding prognostic assessment <sup>[20]</sup>. In laboratory practice, the conventional light-microscopy-based protocol relies on the application of coloured (chromogenic) stains, whose properties determine multiplexing efficiency on serial samples. While recent microscopy advances have enabled multiplex detection on single slides in combination with consecutive denaturation of target sites, cancer-specific interrogations exploit pathological targets undergoing frequent modifications and seldom require more than four biomarkers <sup>[21]</sup>.

Fluorescence in situ hybridization (FISH) represents a cost-effective in situ molecular cytogenetic technique widely employed for treatment stratification, particularly in

metastatic non-small cell lung carcinoma (NSCLC). The assay facilitates the detection of epidermal growth factor receptor (EGFR) amplification and predicts responsiveness to anti-EGFR therapies and associated improved clinical outcomes <sup>[22]</sup>. Developed initially to localize DNA sequences on chromosomes within metaphase spreads, nuclei, and interphase cells, FISH studies cells adhering to their native growing substrate. The technology employs a fluorescence microscope to visualize hybridized genomic sites labeled with a fluorochrome, revealing gene copy number and structural copy number variations such as deletions or translocations <sup>[23]</sup>.

The technique's foundational principle involves the complementary nature of DNA molecules. Genomic DNA in a suspended chromosome preparation, metaphase-spread nucleus, or tissue sample is denatured to separate the strands. A labeled nucleic acid probe mixture is then introduced and hybridized under permissive conditions. Post-hybridization washing removes unhybridized probe, allowing the target DNA to be visualized either directly (with a fluorescent-labeled probe) or indirectly (using a fluorescent antibody affinity system). This approach enables the identification of specific DNA sequences in situ within nuclei or chromosome spreads. Consequently, the methodology offers dual functionality, permitting detailed nuclear and chromosomal analysis.

In addition to imaging and molecular techniques, endoscopy is also used for cancer detection. Endoscopy enables doctors to look at the inside of hollow organs, minimally invasively, with a bright light and a small camera

attached to the end of a flexible tube. It is an important tool in the detection of cancers of the gastrointestinal tract, the lungs, and the bladder, among others.

Cancers of the gastrointestinal (GI) tract include esophageal, stomach, liver, pancreas, small intestine, colorectal, and anal cancer. These cancers can be detected by esophagogastroduodenoscopy (EGD), a biopsy of the liver or pancreas guided by endoscopic ultrasound, or colonoscopy. Lung cancer can be detected with bronchoscopy or endobronchial ultrasound (EBUS). Bladder cancer can be detected with cystoscopy.

The endoscopic examination of various anatomical sites provides direct visualization and enables screening and surveillance of specific cancers. Gastrointestinal cancers are among the five most common worldwide, with gastric cancer being the third leading cause of cancer-related mortality. Early diagnosis of gastric cancer through endoscopy is critical for reducing mortality rates. Conventional white light endoscopy (WLE) remains fundamental for detecting and characterizing gastric lesions, yet it may not reliably diagnose preneoplastic conditions. The European Society of Gastrointestinal Endoscopy therefore recommends image-enhanced techniques—such as magnification chromoendoscopy and narrow-band imaging—to improve the identification of gastric adenocarcinoma and preneoplastic lesions including intestinal metaplasia and dysplasia. Elevated and protruded gastric cancers typically present as irregular, whitish-colored lesions readily observed under white light, with large, irregularly shaped, reddened areas exceeding 2 cm in

diameter suggesting malignancy. Flat or depressed lesions exhibiting irregularities alongside reddish or whitish discoloration are also discernible by WLE. Advanced modalities like magnifying endoscopy combined with narrow-band imaging further assist in differentiating malignant from non-malignant tissues by revealing irregular microsurface and microvascular architectures, with biopsy providing definitive confirmation [24]. The recent evolution of optical molecular imaging techniques facilitates real-time detection of morphological and biochemical alterations associated with gastrointestinal neoplasia. Current widefield approaches under clinical and preclinical evaluation include high-definition WLE, narrow-band imaging, autofluorescence imaging, and chromoendoscopy, supplemented by high-resolution probe-based confocal laser endomicroscopy, high-resolution microendoscopy, and optical coherence tomography for enhanced sensitivity and specificity in colorectal and esophageal cancer detection. The clinical imperative for improved detection methods is underscored by the poor prognosis of late-stage colorectal cancer and the rapidly increasing incidence of esophageal adenocarcinoma worldwide [25].

Lung cancer is the second most common cancer worldwide. Detection methods include CT scans and biopsy via bronchoscopy. Bronchoscopy is most commonly used when the tumor is close to the opening of the lung, where the abnormal cells can be visualized and a sample collected. Endobronchial ultrasound (EBUS) is a minimally invasive technique that helps locate and obtain lymph nodes for sampling, and an ultrasound-guided very thin bronchoscope

combined with a navigation system is employed to reach and biopsy tumors located in the very deepest part of the lungs.

Doctors insert a thin, flexible, lighted tube with a camera on the end called a bronchoscope through a patient's nose or mouth and down the airway into their lungs to perform these tests. The bronchoscope lets a doctor see inside the lungs. They are often used when an abnormal area is seen on a chest CT scan and a sample of the tissue is needed.

Most bladder cancer cases are detected by diagnostic methods prompted by hematuria. Cystoscopy serves as a minimally invasive, gold-standard technique, permitting direct inspection and collection of bladder tissue for diagnostic examination. White-light cystoscopy (WLC) is the standard procedure, complemented by ultrasound, computed tomography urography, and magnetic resonance imaging (MRI). All imaging techniques except WLC are unable to detect subtle urothelial changes and small structural bladder tumors. WLC has limitations such as inability to grade cancer stage and detect early flat cancer at stage carcinoma in situ (CIS). Small tumors, satellite lesions, and CIS are frequently missed, yet these are linked with high early recurrence rates. Contrastingly, ability to predict tumor stage or grade based on appearance remains limited. Real-time pathological information during cystoscopy could therefore substantially improve assessment, distinguish inflammatory lesions from CIS, and optimize resection strategy. Fluorescence cystoscopy employing an intravesical photosensitizer addresses these needs by enhancing tumor visualization, improving

specificity, and permitting instantaneous, image-guided tumor diagnosis through precise excision. Although WLC remains the current diagnostic standard, new optical techniques aim to increase detection sensitivity, lower recurrence rates, and facilitate early-stage diagnosis <sup>[26, 27]</sup>.

Blood-based tests are a cornerstone of early cancer detection. Several blood markers change as a result of cancer or pre-cancerous conditions and are frequently measured for clinical indications such as blood concentration, blood clotting, and organ function. Widely ordered tests, including complete blood counts (CBC) or liver function tests, are frequently recommended for screening purposes alongside a physical examination. Despite the absence of formal recommendations for general screening beyond physical exams, tumor markers are blood markers directly associated with tumors and are regularly measured when cancer is suspected.

Blood markers play a significant role in monitoring chemotherapy and radiation treatments for cancer patients. Consequently, accurate measurement of these markers can reduce the number of follow-up scans required and improve the precision of longitudinal tracking <sup>[28]</sup>. Blood markers represent an early and accessible detection method that addresses some of the limitations in more general population screening <sup>[29]</sup>.

The complete blood count (CBC) is a routine laboratory test frequently performed in the clinical setting and particularly relevant for cancer screening <sup>[30]</sup>. CBC measures the blood-cell composition and evaluates the size, quantity, and maturity of each type of blood cell to predict



abnormalities or malignant processes related to cancer <sup>[31]</sup>. Blood cells can be divided into three broad categories: erythrocytes (red blood cells), leukocytes (white blood cells), and platelets. Erythrocytes are responsible for oxygen and carbon-dioxide transport and play a principal role in cellular metabolism. Leukocytes lead the immune system and initiate the body's physiological response to counter infection. Platelets are responsible for blood-clotting mechanisms and initiate the thrombus formation to seal infected areas and avoid further infection <sup>[32]</sup>. Leukocytes represent approximately 0.1% of the total blood volume and can be categorized as neutrophils, lymphocytes, and monocytes. Neutrophils prevent the body from pathogenic microorganisms and play an essential role in innate immune defence by phagocytizing infectious organisms. Lymphocytes trigger an antibody-mediated immune response when exposed to infectious organisms. Monocytes are phagocytic cells and protect the body from viruses and intracellular bacteria. Various parameters from a CBC panel can be applied to diagnosis because cancer development affects the integrity of organs and the immune system. Therefore, when cancer spreads to other organs or the immune system searches for cancer formations, changes in blood-cell counts become measurable, and CBC is a suitable diagnostic screening tool for cancer.

Liver function tests are important indicators of liver injury and play a meaningful role in the screening of liver cancer <sup>[33]</sup>. The early diagnosis and treatment of liver cancer are very important for prolonging survival and improving life quality. Serum tumor markers, such as alpha-fetoprotein

(AFP) and CA199, can help detect abnormalities early, but their sensitivity and specificity are limited, and they are not exclusive to liver cancer. Imaging technology plays a key role in early screening and diagnosis. Contrast-enhanced ultrasound can more accurately display blood flow, lesions, and differences between benign and malignant liver conditions without radiation exposure, and has a higher detection rate than enhanced computed tomography (CT). Enhanced CT provides high tissue resolution but may cause misdiagnosis due to overlapping features with benign lesions. Combining contrast-enhanced ultrasound, enhanced CT, AFP, and CA199 improves diagnostic accuracy and sensitivity, making early clinical diagnosis more reliable. The combined detection approach shows significant promise, with higher sensitivity and accuracy than single methods, but larger sample sizes are needed for further validation.

Tumor markers comprise a diverse group of molecules that signal the presence, progression, or treatment response of malignant tumors <sup>[34]</sup>. These substances include proteins and other molecules secreted by tumors, enzymes involved in malignant transformation, products of host environmental response, and molecules indicating disturbed immune function. High predictive/diagnostic value, ease of measurement, and cost-effectiveness describe an ideal tumor marker; as yet, no such universally applicable marker exists. Nevertheless, many tumor markers play vital roles in cancer management. Multiple markers—often interpreted collectively—guide clinical decisions, and important markers have established roles in various malignancies. Tumor markers currently contribute to screening early-stage

malignancy, differentiating benign and malignant diseases, assessing prognosis, performing postoperative surveillance, predicting therapy outcomes, and monitoring response to systemic treatments.

Emerging technologies in cancer detection encompass liquid biopsy methods such as circulating tumor DNA (ctDNA) and whole blood/Buffy coat analysis, artificial intelligence (AI) applications in diagnostic imaging, and nanotechnologies including nanoparticle usage and exosome investigations [3].

Liquid biopsies have emerged from concepts surrounding ctDNA and circulating tumour cells. Compared with imaging approaches, they are potentially more sensitive than tissue biopsy and facilitate serial sampling. A 2023 discovery refining the concept involves a computational analysis algorithm followed by multiparameter deep evaluation of the immune profile.

Machine learning methods driven by AI applied to imaging data can assist in the integration of information from multiparameter sets and correlate automatically with existing medical knowledge. Deep learning approaches show promise in reducing false-positive interpretations in interpretive imaging, such as mammography, through the combination of hundreds of thousands of annotated images with multi-institutional data and synthetic data generation.

Nanoparticles addressing limitations imposed by competing biological interactions have been developed to target the tumor microenvironment with high specificity and to diagnose and intermittently treat the target. Advantages include reduced risk of insufficient tissue and false-negative

results by providing a continuous low-dose supply of biomolecules that can be continuously monitored by magnetic particle quantification with a portable device.

An emerging method for cancer detection, liquid biopsy focuses on the acquisition of tumor cells or tumor biospecimens circulating in blood and other bodily fluids, or the tumor-released markers contained therein, such as circulating tumor cells (CTCs), cell-free circulating nucleic acids, extracellular vesicles, and proteins <sup>[35]</sup>. Conventional tissue biopsy analysis may be prone to sampling bias; furthermore, tissue biopsies are invasive and cannot be easily repeated, whereas liquid biopsy components more reliably represent spatial and temporal intratumoral heterogeneity and therefore may be utilized for longitudinal monitoring of cancer development and resistance <sup>[36]</sup>. Under these conditions, liquid biopsy offers potential for early diagnosis, prognosis, surveillance, treatment-efficacy evaluation, and evaluation of therapeutic targets <sup>[28]</sup>.

Artificial intelligence (AI) systems can greatly improve image-based cancer diagnosis by assisting with tasks such as tumor detection, segmentation, and classification. AI algorithms perform organ or lesion detection to identify and delineate regions of interest. End-to-end detection systems can automatically discover the most salient features directly from images and eliminate the need for separate processing steps or prior knowledge. Convolutional neural networks extract hierarchical features describing the relationships among adjacent pixels or voxels <sup>[37]</sup>.

Deep learning architectures enable automated staging and facilitate reliable classification based on learned feature

representations. AI models can analyze large datasets to differentiate benign from malignant tumors, predict survival rates, and incorporate diverse information streams such as biomarker and molecular signature assays into the overall risk assessment. Enhanced image-processing techniques, including phase-contrast imaging, support radiologists in cancer detection and classification while helping to reduce patient burden and clinical costs <sup>[38]</sup>.

Nanotechnology is at the forefront of fundamental advances in science and has the potential to reshape the landscape of cancer detection and treatment <sup>[39]</sup>. Despite the widespread occurrence of dedicated cancer diagnostics in the health market (e.g., pregnancy tests), nanotechnology continues to be relatively underutilized in routine clinical approaches. The influence of drug delivery, however, has been considerable. Early detection of cancer is paramount when assessing the severity of the disease and prognosis since survival is closely tied to the ability to diagnose the cancer at an early stage. Current detection and monitoring methods permit the identification of cancer when the lesions have grown large enough to induce macroscopic anatomical or physiological modifications. Imaging techniques such as X-ray, computed tomography (CT), magnetic resonance imaging (MRI), endoscopy, and ultrasound can only detect cancer when there is a sufficiently large number of abnormal cells to generate a visible structural change. Cytology and histopathology take over where imaging falls short, yet they remain poorly suited for the diagnosis of early-stage cancers or for detecting single or few cancerous cells. Nanotechnology offers attractive opportunities to bridge the

gap between detection and imaging in cancer diagnosis. Nanobased approaches can capture several types of cancer indicators, including proteins, circulating tumor DNA, circulating tumor cells, micro-RNA, and exosomes. Small-volume liquids may also be analyzed, and nanoparticles provide a large surface area to volume ratio, supporting the dense coating of specific recognition molecules. The prospects for novel diagnostic methods that permit real-time, on-site, and cost-effective cancer diagnosis are excellent; however, significant challenges lie ahead to fully meet the demands placed by clinical cancer diagnostics.

Cancer screening offers the opportunity for early cancer detection in asymptomatic individuals. Anti-cancer treatment at an early disease stage is often associated with better outcomes and a higher chance of survival (Magee *et al.*, 2003). Screening aims to detect disease at an early stage and to offer diagnostic confirmation and treatment to individuals diagnosed with the disease. Effective screening programs also provide health education to participants, raise awareness of symptoms, promote healthy lifestyles, and deter tobacco smoking and excessive alcohol consumption.

In current clinical practice, caution is advised when interpreting a normal screening test result because it neither definitely excludes malignancy nor guarantees immunity from future development of cancer. Patients are advised to remain vigilant about cancer-related symptoms and to seek early medical care should symptoms emerge. Most cancer screening guidelines recommend well-established procedures such as mammography for breast cancer, Pap smear for cervical tumors, and colonoscopy for colorectal

cancers. Screening programs should commence at specific ages, typically around 50 years, coinciding with the increasing incidence of malignancies in middle-aged and elderly populations. Guidelines suggest individualized consideration of screening tests for patients outside the recommended age range who possess one or more risk factors for cancer development.

Age is the most important risk factor for developing cancer; around 80% of all cancers in the Western world occur in people aged 55 or older. Despite this, media and cancer organizations continue to emphasize the risks of cancer mainly for young people <sup>[40]</sup>. The risk of cancer varies by site and sex; for instance, men carry up to a 43% lifetime risk of receiving a prostate cancer diagnosis versus breast cancer's 12% risk for women. While most screening protocols recommend different screening methods based on age or family history, there are clear exceptions: 35-year-old women are advised to undergo Pap smears, despite cervical cancer's low incidence across all age groups and the absence of evidence supporting screening under 25 years of age. This is, however, the youngest recommended patient population to be screened for cancer, which constitutes a public health milestone.

American Cancer Society recommendations for test use by cancer and risk group are summarized below. Specialist consultation may be appropriate for further evaluation and for assessing suitability of screening for rare cancers <sup>[41]</sup>.

Cancer mortality and incidence are increasing worldwide, with predictions of 30 million annual deaths by 2030 <sup>[39]</sup>. Early detection is key to reducing cancer-related

deaths, exemplified by breast cancer's high 5-year survival rate when detected early. Despite existing modalities, several challenges remain. Procedures can be invasive and cause discomfort. Imaging techniques such as MRI, CT, X-ray, endoscopy, and ultrasound detect cancer only after visible changes occur, often when the disease has proliferated or metastasized. They cannot effectively distinguish benign from malignant lesions, and cytology and histopathology have limitations for early detection. Blood tests can be inconclusive because physiological changes may arise from other causes. Low- and middle-income countries experience a disproportionate burden of cancer deaths, highlighting the need for better availability and cost reduction of current techniques <sup>[3]</sup>.

False-positive and false-negative results arose throughout cancer history, often producing either unnecessary intervention or failure to implement early life-extending treatment. High rates still dominate across several widely used diagnostic tests.

Histopathologic techniques often ensure an established molecular or endoscopic detection. Their increased skill and knowledge-intensive nature can manifest greater false rates for some cancer types. Moreover, several cases produce unequivocal results signifying sample recount and retrieval. Prostate cancer exemplifies the difficulties, since Gleason 1 and 2 did not correspond to valid patterns <sup>[42]</sup>. Large-scale study of biopsy tissues further identified the adenosis mimicker as the leading diagnostic discrepancy cause. False-positive rates from early work were markedly greater because of that disparity. Interpreting



immunohistochemistry (IHC) for individual glands separately rather than the population level also induced errors. Targeted training and external quality assessments might reduce incidental misinterpretation.

Low-dose computed tomography (LDCT) achieves unprecedented accessibility, but its limitations remain a substantial concern. Multiple case studies reinforce the far-reaching consequences of a single false-negative instance. Direct costs increased sharply with the stage of diagnosis, from \$161,116 at stage 1 up to \$418,591 for stage 4 <sup>[43]</sup>. Hospital systems also encounter geometric growth in malpractice liability expenses. The most common malpractice complaint corresponded to delayed diagnosis or treatment initiation, representing 82% of breast cancer claims with average settlements of \$978,910. Research thus emphasizes the necessity of explicit patient education on LDCT's shortcomings. Cancer occurrence frequency and heightened malignancy between scan intervals initiate the highest risk.

While screening programs offer some reassurance, approximately half of patients with early symptoms do not consult their physician within the first month following onset <sup>[44]</sup>. Among those who do seek medical intervention, a third will not be suspected of having cancer or be appropriately referred. Even when suspicion arises and investigations are appropriate, facilities may not be locally available and outcomes may be compromised by delays <sup>[45]</sup>. Delayed consultation and diagnostic processes can lead to presentation at more advanced, less treatable stages of cancer.

Disparities in access to clinic- or hospital-based screening programs result in significant disparities in the quality of cancer treatment available, particularly along social class lines and in geographical accessibility. If screening is to fulfill its objective of reducing the burden of cancer and allowing systematic monitoring at the population level, systems need to be designed for universal coverage. Screening generally requires professional administration in a clinical setting and requires subsequent access to confirmatory diagnostics and treatments. This approach carries an inherent risk of neglecting populations that are hard to reach due to social and/or geographic reasons. Alternatively, offering widespread access to tests among healthy individuals without adequate professional input to interpret results is unsatisfactory, opening the possibility of unnecessary anxiety or poor reassurance.

Several factors combine to discourage access to screening among hard-to-reach groups. First, the individuals are often unaware that screening is an option as well as why it might be valuable. Second, some groups tend to distrust the healthcare system or scientific community and are therefore reluctant to engage. Third, as most screening requires professionals and the marking of appointments during office hours, individuals in underprivileged jobs find accessibility difficult. Strategies developed to improve access include offering extended opening hours, developing “pop-up” clinics in non-traditional settings, delivering a more culturally sensitive approach to ‘demystify’ screening, integrating screening alongside other interventions of value to the population, and providing tests for self-administration.

Without cost control, any attempt to make a screening or diagnostic test widely available results in consumption so high that the financial survival of the health-care system cannot be guaranteed <sup>[46]</sup>. The role of cost-effectiveness in cancer diagnosis must therefore be considered at the population level as well as at the individual level. Diagnostic tests may have a place because their use leads to the application of other technologies or therapies that have a high probability of success with acceptable associated costs. Imaging has a tremendous role to play in this respect.

Test cost is clearly part of the cost-effectiveness equation. Other components include the costs of the disease process and subsequent interventions, probability of disease, and the effect of the test on outcome measures such as survival. In population screening, the aim is to reduce the number of endpoints associated with the natural history of the disease; these endpoints include death, relevant clinical events (e.g. metastases or loss of organ function), and the activation of treatment. From the public-health perspective, the picture is further complicated by the need to maintain and improve quality of life, avoid anxiety or distress, and to offer an equitable approach to all.

Frequent use combined with the relatively high cost of imaging examinations has recently placed the spotlight on imaging in discussions about the escalating costs of health care. The replacement of simpler techniques with more sophisticated methods has questioned the cost-effectiveness of contemporary diagnosis, which prompts an exploration of the requirements for cost-effective cancer imaging linked to recent developments in the clinical practice of oncology.

The evaluation of new technologies is important, especially as this indicates that current practice is less than optimal and considerable scope exists for change.

The current suite of established cancer detection technologies enables the routine detection of cancers across diverse anatomical sites at clinically relevant stages. Research and development efforts are increasingly focused on achieving the next level of improvement, which is early detection of cancers at pre-invasive and precursor stages. The development of such technologies will occur over a long timeframe, because of different research approaches and increasing stringency of regulatory environments. Nevertheless, many factors including high unmet clinical needs, available technologies, regulatory incentives, and interest from public funding bodies and private investment favor accelerated progress. Early-detection tools will almost certainly be far more effective if deployed as components of integrated approaches, in which multiple platforms (genetic, imaging, blood-based, and those based on other biospecimens) work synergistically to identify lesions of the greatest clinical significance. Collection of complementary, spatially resolved molecular and histological data will make it easier to characterize the current properties of tumours and to predict their likely future behaviour. Additional new platforms, such as analysis of breath, exhaled volatile metabolites, or body odour, may find a place, and the deployment of machine learning across the spectrum of screening, detection, diagnosis, prognosis and treatment selection will lead to a rapid increase in power and specificity [3].

The integration of omics techniques has consistently driven new directions in the detection of cancer. Each of the traditional biopsy and screening techniques offers unique insights, probing different molecular layers of cancer. Histopathological methods assess tissue morphology, molecular techniques survey genomics and transcriptomics, endoscopic methods visualize the site of disease and blood tests monitor tumor markers. The combined molecular assessment of cancer can therefore be achieved by incorporating transcriptomics, genomics, epigenomics and proteomics in clinical workflows. Beyond the traditional techniques, the emergence of metabolomics and metagenomics has further expanded the multi-omics arsenal, offering additional layers of molecular insights into cancer.

Contemporary frameworks for effective cancer detection leverage the voluminous multi-omics data recently generated across cancers. Despite the diverse methods through which this data is harvested—whether blood, tissue, faecal, metabolite or microbiota samples—the application of machine learning to multi-omics datasets is paving the way towards cutting-edge detection approaches with improved patient outcomes. The ongoing challenge is to translate these research advances into clinical settings, where resilience to population-specific variables such as ethnicity, locality and diet remains to be conclusively demonstrated.

Personalized screening strategies modify testing frequency and selection based on individual risk profiles. Factors shaping recommendations include a person's age,

family history, genetic predisposition, prior screening results, lifestyle, and environmental exposures, which reflect both innate and exogenous components of cancer risk [41]. For example, women who carry BRCA1 or BRCA2 mutations are generally advised to begin mammographic screening at age 30 instead of the conventional age of 40. Conversely, a history of exposure to coal tar, arsenic, or ionizing radiation prompts initiation of screening 10 years earlier than usual. Guidelines also mandate earlier and more frequent screening for those with a personal history of cancer, given the elevated likelihood of second primary tumors. High-risk categories drive more intensive and regular assessments, facilitating earlier detection.

The detection of cancer is essential for its diagnosis and treatment. Early detection raises the chance of successful treatment, making methods for detection important for primary prevention. Different technologies are applied to various types of cancer, with some being effective for multiple forms. Screening guidelines suggest different examinations according to age, sex, and the affected site of cancer. The most relevant classical methods in clinical practice are presented, highlighting recent advances.

Non-invasive imaging techniques such as X-ray, CT, MRI, and Ultrasound are extensively utilized for tumor screening and detection across different tissues. Traditional methods for cancer detection focus on biological markers, genetic testing, circulating tumor DNA in plasma, endoscopies, histopathological analysis of biopsy samples, blood tests, and other symptom-related examinations. The detection of cancer based on signs and symptoms is closely

related to specific forms primarily associated with pain, bleeding, or unusual discharges. Current challenges and perspectives in cancer detection remain, and recent advances continue to be proposed to improve early-stage detection across all organs.

### **3.1 Limitations of Traditional Techniques**

Microsensors represent an appealing framework for a variety of applications that demand minimal invasive procedures, rapid responses to changing conditions, and user-friendly operation that can be easily utilized in various settings. They are particularly valuable in contexts such as environmental quality control, industrial process monitoring, and early disease diagnosis, where timely information is crucial. Acoustic-wave devices, when effectively combined with molecularly imprinted polymers (MIPs), showcase considerable promise as non-invasive, versatile tools for medical monitoring and other diagnostics. These sophisticated systems can operate similarly to highly stylized electronic noses or tongues, exhibiting excellent stability and specificity in their measurements. An innovative acoustic wave sensor that employs MIPs has been meticulously developed for the precise detection of urinary nucleosides, which serve as critical biomarkers for the early detection of colorectal cancer. The primary aim is to establish a real-time microsensing approach that is capable of reliably detecting tumor markers, even at low concentrations, thus significantly contributing to non-invasive clinical diagnosis practices. Most conventional techniques that exist for early cancer detection tend to be highly invasive and entail lengthy, costly processes that

discourage frequent patient participation in much-needed screening activities. This situation can notably increase anxiety levels during examinations and limit equipment mobility and usability, as well as the potential for patient self-monitoring, which is increasingly becoming vital in modern healthcare. Standard analytical methodologies—such as solid-phase extraction followed by high-performance liquid chromatography with ultraviolet detection (SPE-HPLC-UV), capillary electrophoresis with UV detection (CE-UV), liquid chromatography-tandem mass spectrometry (LC-MS/MS), and gas chromatography-tandem mass spectrometry (GC-MS/MS)—typically require intricate blood collection, extensive sample preparation, the involvement of highly trained personnel, and an overall considerable investment of time and expense. In contrast, portable, miniaturized devices, particularly those that are capable of multiplexed detection and straightforward operation (for example, paper-based analytical devices), have become commercially available and are now more suitable for point-of-care applications. The deployment of such advanced technologies would freely enable on-site evaluations, facilitate timely results, and broaden accessibility, particularly in regions where traditional laboratory infrastructure is severely lacking, thus transforming the landscape of essential diagnostics and patient care [24, 25, 26, 27, 28, 29].



# Chapter - 4

## The Role of Quantum Sensors

Quantum sensors take advantage of the delicate and intricate nature of quantum systems, utilizing them to measure various important quantities, including time, electromagnetic fields, temperature, pressure, and force. The inherent fragility of these quantum systems means that any perturbations can significantly alter the state of the system, and these alterations can be accurately measured to reveal the value of the quantity that is being sought. Because quantum sensors capitalize on the unique properties exhibited by single quantum systems, they achieve sensitivities that far surpass those achievable by classical measurement devices. This remarkable capability allows quantum sensors to uncover minute changes that would otherwise go undetected. Indeed, quantum sensors have already brought about significant transformations in several critical areas of measurement. Notable applications include the observation of gravitational waves, advancements in atomic clock technology, and the development of highly sensitive magnetometers, which are just a few examples of their versatility. In a groundbreaking development, researchers have created a portable quantum sensor that employs a macroscopic quantum device specifically designed to measure cancer biomarker signatures. This

innovative approach presents a fresh and promising technique for early and rapid detection of cancer, potentially revolutionizing how we diagnose this disease. In this context, the quantum sensor functions as a switch, demonstrating a level of sensitivity that is far superior to that of conventional alternatives. For comparison, a standard transistor requires a change in either voltage or magnetic field of only a few millivolts or fractions of a millitesla to be activated, whereas a superconducting quantum switch can be triggered by variations that are five orders of magnitude smaller. This leap in sensitivity opens up new avenues for precision measurements and could make a significant difference in the effectiveness of early cancer screenings [1, 14, 30, 31, 4, 32].

## **4.1 Mechanisms of Quantum Sensors**

Detection purposes rely heavily on advanced quantum sensors, which cleverly exploit essential and fundamental properties of quantum mechanics—such as quantization, tunneling, interference, entanglement, coherence and decoherence, as well as spin—in their sophisticated operation. These properties play a critical role in enhancing the precision and capabilities of detection technologies.

The operational architecture makes use of various entities such as atoms, ions, and molecules, alongside solid-state electronic, vibrational, and rotational states, serving as the fundamental sensing elements for the system in question. The effective size of the sensor, which is of great importance, corresponds directly to the spatial extent associated with the constituent quantum object that it employs. This relationship highlights the significance of

quantum properties in sensor design and functionality [1, 33, 34].

## **4.2 Advantages of Quantum Sensing in Medicine**

Quantum sensing is an innovative and emerging technique that is fundamentally grounded in the advanced and complex principles of quantum mechanics. Quantum mechanics serves as the very foundation for defining and understanding the intricate physical properties of nature. It encompasses essential concepts that are vital to modern science, such as quantization, coherence, and the profound phenomenon of wave-particle duality. Quantum sensors take full advantage of these unique physical properties to effectively reveal the significant challenges and limitations that are encountered when one attempts to reproduce the complexities of nature using classical means alone. These remarkable sensors are capable of detecting single fundamental quanta—these include particles such as photons, electrons, atoms, and even molecules themselves. They rely heavily on the ingenious exploitation of distinctly quantum properties, including entanglement, superposition, and squeezing, to significantly enhance their overall functionality. As a direct result of these properties, quantum sensors exhibit extraordinarily high levels of sensitivity and precision. This makes them distinctly superior to conventional sensing technologies that are reliant on classical principles. Portable quantum sensors present particularly noteworthy advantages, especially in the critical realm of early cancer detection. By strategically placing these advanced sensors alongside patients, healthcare providers are empowered to receive timely alerts and

accurate diagnoses. This capability allows for prompt medical intervention before the cancer progresses to a stage beyond the possibility of cure. The early detection capability afforded by quantum sensors can significantly improve patient outcomes and optimize treatment strategies in ways that were previously unimaginable. Numerous experimental studies have robustly demonstrated the effectiveness of quantum sensors by successively harnessing the intricate interactions between quantum bits (qubits) and their local environments. This groundbreaking research is effectively paving the way for the development of a new generation of highly sophisticated and efficient quantum sensing devices. These devices hold the potential to transform various essential fields, including medical diagnostics, environmental monitoring, and even beyond those realms. The ongoing advancements in quantum sensing technology are filled with great promise for the future. Researchers are tirelessly continuing their explorations and pushing the boundaries of what is possible within the truly fascinating realm of quantum mechanics, opening up a myriad of possibilities that could revolutionize our understanding and interaction with the world around us [1, 31, 3, 4, 35].

# **Chapter - 5**

## **Design and Development of the Portable Quantum Sensor**

The innovative and advanced device that has been developed combines dual measurement capabilities with impressive portability, which makes it highly suitable for on-site or point-of-care applications. This is especially important in resource-limited settings, where traditional laboratory equipment might not be accessible. It is essential to clarify that this device is not intended to serve as a replacement for conventional benchtop spectrometers; rather, it provides a practical alternative that focuses on targeted measurements which do not necessitate detailed or extensive spectral information. The advanced capabilities that have been developed for detecting reflectance could be directly applied to a portable quantum sensor, which would significantly enhance its functionality. This feature would complement the already demonstrated capabilities of fluorescence detection. By incorporating reflectance measurements, the device would enable a broader range of real-world applications, including the critical task of assessing haemoglobin concentration during attempts to diagnose breast cancer. By blending these diverse disciplines, the combination allows for the creation of a truly unique medical device that can quickly and effectively

assist in the diagnosis and analysis of breast cancer. This device remains simple enough for wide deployment, making it an invaluable tool in the field of medical diagnostics, particularly in scenarios where immediate results are needed, facilitating timely interventions for patients in various environments [36, 37, 38, 39, 40].

Quantum sensors employ a quantum system and exploit quantum correlations to perform measurement tasks. A combination of coherence, interference, and entanglement results in measurement sensitivity that can considerably surpass classical systems [1]. Portable quantum sensors are particularly promising, since they combine improved performance with increased mobility and deployment flexibility. The design and development of this type of sensor are a key enabling step toward next-generation sensing devices.

Quantum sensing finds a wealth of applications in many different fields. For instance, ultra-precise quantum-based measurements of magnetic and electric fields are well-suited to studying biological systems, since these signals carry immediate, useful information about electrophysiological processes. Atomic sensors make it possible to measure time and frequency, with an outstanding level of precision. Accurate measurements of gravitational fields are crucial in geophysics and ventilation-leak detection. Portable navigation systems become viable in cases where global positioning system (GPS) signals cannot be received, or where higher precision is required. Distributed quantum sensing substantially enhances sensor networks, opening new directions in quantum metrology, while quantum

imaging can, at least in principle, achieve a spatial resolution beyond the Rayleigh criterion.

Quantum sensors exploit various quantum phenomena—such as entanglement, squeezing, and superposition—to achieve performance exceeding that of classical devices <sup>[1]</sup>. The quantum advantage arises primarily because electrically small devices can exhibit sensitivity superior to classical sensors of similar scale <sup>[2]</sup>.

Using the quantum sensor concept as a foundation, developing design principles for portable variants becomes necessary. Investigating the fundamental physical characteristics of particles forms the first step in this process.

Early in the 20th century, experiments revealed that all waves exhibit particle-like behaviour, all particles exhibit wave-like behaviour, and that these phenomena are associated with an intrinsic indeterminacy in the outcomes of measurements. The nature of physical reality was questioned, and the language of classical mechanics was replaced by the formalism of quantum mechanics. It is now accepted that no matter how great the skill of an observer, the outcome of a single measurement on any simple physical system of any basic physical quantity is profoundly uncertain. When describing how systems evolve with time, probabilities evolve deterministically, and measurement of one variable can influence others without classical interactions. No physical quantity has a definite value until measured. Quantum mechanics is essential for building models that replicate experimental behaviour.

Quantum-mechanical principles describe the behaviour of individual particles and collections of particles. It is common to use the term state to denote the quantity encompassing all quantum-mechanical information about a particle (or system). Quantum states are found by solving either the Schrödinger equation or appropriate relativistic equivalents. Some useful quantum-mechanics facts provide a foundation for the following sections. All dynamical variables—including electrical quantities such as voltage, current, and magnetic fields—satisfy quantum-mechanical rules. The quantum impedance of the waveguide modes sets a fundamental limit to the sensitivity of any sensor. Devices thereby approach the individual-quantum-particle limit of detection. Quantum sensing involves the interaction between the quantum states of the target and sensor, which evolve mutually over time.

The role of sensors for the modern world can hardly be overstated; they enable the measurement of various physical parameters such as temperature, pressure, and magnetic fields. As many domains transition towards autonomous or smart systems, the need for sensors capable of operating without human intervention will inevitably grow. Typically, one makes a distinction between classical and quantum sensors: Classical sensors, which can be mechanical, chemical, or electronic, function by interfacing with a classical environment. Classical limitations eventually occur primarily because of noise and precision restrictions, which emerge as the size of the sensor shrinks. In turn, quantum sensors interact directly with quantum mechanical objects. Therefore, they tend to be more sensitive relative to



their classical counterparts and can detect smaller amounts of physical phenomena such as electric fields or environmental changes <sup>[1]</sup>. Although those requirements seem to imply bigger and bulkier devices (e.g., ion traps or cold-atom clouds require laser pumping), recent progress within quantum computing and condensed matter physics provides a promising outlook. Thanks to such interdisciplinary advances, a viable approach to design a portable quantum sensor is now within reach <sup>[2]</sup>.

Classical sensors transduce physical variables into measurable signals and have been widely used in various fields. Classic examples include accelerometers and gyroscopes in navigation, where microelectromechanical systems (MEMS) accelerate a proof mass in the sensor under tilt or rotation. The relative motion between the sensor frame and the proof mass is measured through piezo-resistive, piezo-electric, and capacitance variations, or atomic spectroscopy. Mems-based sensors generally have a high bandwidth and low weight, volume, and power consumption. The average acceleration can be measured over a broad frequency spectrum. Classical sensors also include accelerometers and gyroscopes operating on optical phase shifts. Fiber optic gyroscopes that rely on the Sagnac effect measure the relative phase shift between two beams traveling in opposite directions in the fiber. This technology has been applied to design highly stable accelerometers and gyroscopes <sup>[1]</sup>. When increasing the device size, professional measurement systems reach very high sensitivity and precision, but also have high weight, volume, and power requirements. Some sensors, based on atom

interferometry, have demonstrated sensitivities better than 10 mol in characterizing accelerations, rotations, and magnetic fields. These vacuum-tube sensors do not comply with the requirements for personal use and especially autonomous operation such as parcel tracking. MEMS sensors have relatively high long-term bias drift and noise sensitivity, clock stability remains a challenge, and magnetic sensors exhibit scale factor instability and small charge mobility <sup>[3]</sup>. MR technology provide a low-size scalable design that translates to low cost and low weight. However, MR accelerometers, being velocity sensors, often exhibit drift 10-30 times the gravimetric acceleration, and a combination with an inclinometer is required for tilt sensing. They cannot consequently provide a complete MEMS alternative. Similar considerations apply to magnetoresistance magnetometers.

Advances in quantum sensing have led to compact, portable devices capable of measuring physical quantities such as time, velocity, acceleration, and electromagnetic fields with high precision. Portable quantum sensors utilize quantum phenomena—including coherence, entanglement, and spin-squeezing—to surpass the fundamental noise limits inherent in classical measurement strategies. Recent implementations of low-depth, parameterized quantum circuits with optimal input states and measurement operators approach the fundamental quantum limits within a factor of 1.45, outperforming conventional spin-squeezing by a factor of 1.87 and providing a 1.59-fold reduction in the number of averages required to achieve a given precision. Additionally, on-device quantum-classical

feedback optimization facilitates self-calibration of the quantum sensor, enabling operation without prior knowledge of the device or noise environment <sup>[1]</sup>. Chip-scale quantum sensors based on micromachined atomic vapor cells can interrogate microfabricated vapor cells at distances of approximately 10 m and measure Earth's magnetic field with a sensitivity of about 1 pT/ / • Hz. Simultaneous time-of-flight measurements yield the distance between the microcell and the sensor, correlating position and magnetic field to enable mapping of remote or hard-to-access magnetic fields in unshielded environments with high sensitivity and spatial resolution <sup>[3]</sup>.

The performance of a quantum sensor is critically dependent on the sensor's inherent sensitivity and precision <sup>[1]</sup>. Quantum-physical principles have the potential to improve the accuracy of a given measurement. Quantum sensors provide an inherently higher sensitivity and precision than their classical counterparts, yet quantum resources are extremely fragile. The suppression of noise therefore <sup>[2]</sup>, becomes advantageous when developing a quantum-sensing system. The precise design of a quantum sensor depends on the operating parameters of its underlying model. For a broad variety of critical parameters, environmental disturbances such as temperature or electromagnetic fields are monitored as a function of time. Any violation or deviation beyond permissible limits that these parameters may encounter during the operation can be detected immediately by the sensor. A critical objective in the design of quantum sensors is to reduce the size, power consumption and complexity of the desired system while

maintaining adequate accuracy for the targeted application. The successful design of a quantum sensor is advantageous for several applications such as medical diagnostics, environmental monitoring and communication.

The sensitivity and precision of quantum sensors are inherently linked to fundamental quantum mechanical principles. The incorporation of quantum enhancement techniques, such as entanglement, offers a pathway to approach the fundamental precision limits prescribed by quantum physics <sup>[1]</sup>. By implementing low-depth, parametrized quantum circuits that generate optimal input states and measurement operators, sensors achieve operation close to these limits. This approach notably reduces the number of averages required to attain a specific Allan deviation, outperforming conventional spin-squeezing methods and facilitating efficient precision.

Arbitrary frequency resolution represents another key aspect of quantum-sensor precision. Utilizing the electronic spins of nitrogen-vacancy centers in diamond enables the detection of oscillating magnetic fields with frequency resolution as fine as 70  $\mu\text{Hz}$  over a MHz bandwidth, with continuous sampling preserving sensitivity <sup>[4]</sup>. Frequency estimation capabilities depend primarily on the stability of the external reference clock and the duration of the measurement. Through quantum lock-in detection, signals are stroboscopically sampled while the wideband spectrum can be reconstructed using compressive sampling techniques. Experimental records demonstrate frequency resolution of 70  $\mu\text{Hz}$ , precision of 260 nHz, and signal-to-noise ratios exceeding 10,000 over multiple hours. These

performance characteristics extend the applicability of portable quantum sensors to domains such as magnetic resonance spectroscopy, quantum simulation, and sensitive signal detection.

In addition to high-precision measurement schemes, techniques for noise reduction are pivotal in enhancing the performance and reliability of portable quantum sensors <sup>[5, 6]</sup>. The prevailing experimental platforms underpinning these sensors are also conducive to the implementation of noise mitigation strategies. The fundamental properties of optical fields and the inherent stiffness of trapping geometries in optomechanical systems engender diminutive thermal noise at ambient temperature and pressure, thereby inherently amplifying the signal-to-noise ratio. To further augment the interrogation time within real-time Cartesian tracking, the deployment of a nano-torsional optomechanical approach, as delineated in, is recommended. This configuration substantially enhances sensor geometry and actuation precision, facilitating superior operation and noise abatement. Complementing this, advancements in applied physics and laser science envisaged for the upcoming decades promise to extend portable quantum sensor operating times by two to three orders of magnitude relative to the current domain, thereby significantly elevating sensitivity and signal acquisition capabilities. Pursuit of the highest possible field-sensing performance therefore impels rigorous noise attenuation methodologies.

Exploration of the quantum nature of matter has spawned quantum technologies such as quantum sensing.

The relevant quantum effects exhibit remarkable sensitivity to external parameters setting ultimate limits on achievable precision, well beyond the limits of classical approaches <sup>[1]</sup>. Quantum sensing aims at encompassing a range of emerging quantum technologies that can be employed to enhance studies in physics, food sciences, agriculture, medical sciences, geology, biology, defense, and security <sup>[3]</sup>.

The development of conventional sensing systems based on semiconductor materials is mature, but sensing devices based on quantum materials are just starting. Recent advances in integrated photonic circuits using alkali vapors have paved the way for the realization of quantum sensors. Key considerations in design and development of sensing devices involve high sensitivity, compactness, and the capability to perform onsite measurements in a timely manner. Employing integrated vapors, either in fiber, hollow-core photonic fibers or in cladded photonic integrated circuits, addresses requirements regarding spatial resolution and precision. This fast-growing area and supporting building blocks for such development have considerable value in engineering and science.

Design and development of quantum sensors must focus on optimal sensitivity while ensuring compact dimension: micro- and nanosystems are preferred rather than large and complex sensing schemes <sup>[7]</sup>. Construction of the sensor requires the implementation of a suitable quantum material. Single-molecule magnets appear as promising candidates offering a robust setting for magnetic sensing. The basic building blocks of devices include the quantum materials (quantum dots), the integrated superconducting circuit, and

optical sensing components. Theoretical insights assist in the planning of the design, while successful application calls for extensive tests on a variety of scenarios and environments.

Quantum dots are photoluminescent semiconductor nanoparticles typically capable of emitting light at a given wavelength upon excitation <sup>[8]</sup>. In 1957, semiconductor quantum dots were theoretically described following the discovery of quantum-well states in thin metal films <sup>[9]</sup>. Their application to sensing is a relatively recent development. The first demonstration of quantum-dot sensing was published in 2006 by the group of Lu at Stanford University, who employed CdSe quantum dots to monitor electron transfer through cytochrome c. Ultrafast electron transfer from the CdSe quantum dots to cytochrome c was observed in picosecond time scales when the oxidation state of the protein changed from  $\text{Fe}^{3+}$  to  $\text{Fe}^{2+}$ . The intensity of the photoluminescent luminescence is modulated by the electron transfer event, which in turn is dependent on the redox state of the protein. The researchers developed a system wherein electron transfer from quantum dots governed the reduction of hydrogen peroxide, demonstrating the exploitation of electron transfer catalysis for sensing applications. Various optimizing factors have been widely studied. Composition and shape modulations of the quantum dots allow adjustments of the band-gap energy and surface free energy to achieve high sensitivity and selectivity for specific targets. Surface modifications can prevent non-specific adsorption and the limitations arising from tissue light penetration depth for *in vivo* applications.

The specificity of the sensing modality is also a tunable parameter: many recognition groups such as peptides, antibodies, or ligands can be introduced onto the surface of the quantum dots to target specific analytes.

Superconducting sensors feature prominently in quantum sensing because superconductivity occurs on an energy scale of about 1 meV, whereas typical semiconducting devices have energy scales nearer 1 eV. Superconducting sensors therefore can measure signals that are much fainter. Their additional superconducting properties of near-zero resistance and non-linear kinetic inductance facilitate several detector technologies. Transition edge sensors (TES) exploit the steep superconducting-to-normal transition to achieve high sensitivity and low noise, making them valuable for locating, counting, and calibrating incident photons with excellent energy resolution. TES-based bolometers and calorimeters have been deployed in dark matter experiments and cosmic microwave background (CMB) polarization measurements. Kinetic inductance detectors (KID) consist of multiplexible superconducting resonators sensitive to quasiparticles, enabling mass production and broadband single-photon detection capabilities. Superconducting nanowire single-photon detectors (SNSPD) rely on the non-linear kinetic inductance of ultrathin, narrow superconducting nanowires to sense individual photons with high count rates and low jitter. Superconducting quantum interference devices (SQUID) provide sensitive magnetometry and readout functions; for example, they amplify signals from microwave cavities in axion dark



matter searches. Qubits can serve as sensitive single-photon detectors, and parametric amplifiers offer near quantum-limited signal amplification. Developing such multifaceted technology within contemporaneous constraints requires coordinated fabrication efforts. Fabrication remains a hurdle because device complexity and layers derive unique characteristics from deposition parameters and annealing conditions. Key objectives include achieving lower detection thresholds, larger collection areas, greater sensor counts, and enhanced integration. Collaborative development through research, development, prototyping, and industrial manufacturing is essential to realize future scientific goals <sup>[10]</sup>.

Optical systems within the portable quantum sensor consist of source and detection sections. The source includes a laser diode, birefringent crystals for generating entangled photons, and optics to set the pump beam polarization. The detection section accommodates a quartet of GM-APDs, augmented with polarization beam splitter cubes and liquid crystal polarization rotators (LCPRs) that enable polarization rotation and provide detector redundancy. Integration of the optical unit with the electronics platform is secured using a mechanically robust epoxy suited for space applications. Photon-pair generation rates of approximately 3,500 per second are achieved, limited by low collection efficiency attributed to optical-mode mismatch: the active area of the detectors overlaps only 39% of the pump mode resulting in a 4% photon-collection efficiency. Nevertheless, the signal-to-noise ratio remains sufficient for demonstrating quantum entanglement.

Originally, the optical design included four detectors, with two reserved as backups because of cross-talk arising from optical flashes emitted by the GM-APDs during detection events <sup>[11]</sup>.

Prototyping represents the initial design phase of portable quantum sensors, involving detailed examination of hardware components to define configurations that satisfy functional requirements <sup>[1]</sup>. The process begins with identifying hardware layouts capable of supporting desired operations. Iterative refinement follows, focusing on integrating components such as quantum dots, superconducting materials, and optical elements in a manner consistent with design objectives. Testing and validation constitute the subsequent stage, assessing alignment of operational outcomes with established design criteria. Comprehensive evaluation includes persistence of material properties, consistency of measurement outputs, and durability under simulated deployment conditions. Success is characterized by the capacity of candidate configurations to sustain functional parameters and operational resilience over extended periods without significant degradation.

The design of a suitable quantum sensor begins with the fabrication of a prototype. The original model for this sensor was developed several years ago and tested for its efficacy in building such a device. Unlike the more complex system of the larger prototype, the portable quantum sensor comprises three main components: the quantum sensor itself, a microcontroller, and a real-time clock <sup>[12]</sup>. These elements perform the core functions necessary for the sensor to operate effectively.

The quantum sensor is constructed using a niobium superconducting loop embedded with Josephson junctions. These junctions, implemented via oxidized aluminum barriers, create an energy barrier preventing pairs of electrons from traversing them. Consequently, the niobium loops behave as macroscopic quantum dots. When cooled below their critical temperature through a cryogenic system, typically a Liquid Helium Cryostat, the loops enter a superconducting state exhibiting either a symmetric or antisymmetric Cooper-paired ground state. These states respond differently to environmental changes, and transitions between them generate a current proportional to the external stimulus, which constitutes the measurable output of the quantum sensor.

Validation of the design and development of a Portable Quantum Sensor requires more than presentation of the design criteria, components and development process. Testing of a prototype represents a significant advance toward a fully operational sensor. Tolliver *et al.* provide a thorough description of a Quantum Sensor Field Deployable Prototype. Similarly, testing of the final device forms an essential ingredient in any development process. Natividad *et al.* summarize the Engineering Development process that led to Portable Quantum Technology for Quanterra and Sardana, concluding that the solution offers the capability to overcome many of the limitations of classical sensors.

Quantum technologies will enable sensors to perform even better than their classical counterparts. From an implementational point of view, quantum sensors are not necessarily so different from classical sensors, although in

some cases classical sensors based on superconducting materials offer extreme properties, such as very high sensitivity to magnetic fields. However, quantum sensors require more complexity and sophistication in their design, manufacture and operation. Once this added complexity is appropriately handled, quantum sensors can offer a combination of sensitivity, precision, robustness of operation and portability that surpasses that of their classical counterparts.

Quantum sensors operate at the limits of quantum mechanics for heightened sensitivity beyond classical devices <sup>[1]</sup>. Portable variants offer quantum advantages for a range of applications, including environmental monitoring, medical diagnostics, and navigation.

Miniature quantum sensors reduce size, weight, power consumption, and cost compared to other devices <sup>[3]</sup>. Deployable in remote or hazardous locations, they enable timely monitoring of environmental, chemical, and biological parameters. A compact quantum sensor for medical diagnostics has demonstrated potential to identify infections.

Compact quantum sensor systems are also of interest for navigation. Technologies that provide accurate inertial positioning and timing could enable extended autonomous operation when GPS signals are denied or denied access.

Quantum sensors leverage a wide range of physical quantum phenomena to surpass the performance of their classical counterparts through quantum correlations such as squeezing and entanglement, as well as the quantum

coherence inherent in superposition. In addition to enhanced sensitivity with high spatial resolution, quantum sensors offer ultra-high precision unaffected by drifts, making them indispensable for data acquisition tasks. The maturation of device fabrication and packaging technologies is a prerequisite for rendering quantum sensing technology portable and operable in uncontrolled outside environments.

The principal of locality underscores the appeal of quantum sensors, highlighting the drawbacks of conventional large-scale detection devices that necessitate bulky structures for high-sensitivity measurements. Building a portable quantum sensor entails miniaturizing the core quantum system, minimizing classical control processors, and integrating noise-rejecting schemes to guarantee high sensitivity and accuracy. Design principles encompass sensitivity, precision, dynamic range, and frequency range. Key components include microscopic quantum systems, superconducting technologies, low-noise technologies, and systems capable of amplification, manipulation, and free-space propagation of quantum signals. All facets of prototyping, testing, and applications operate in alignment with these principles. Applications span environmental monitoring, medical diagnosis, disease treatment, and navigation.

Chemical and bio-sensors have been widely studied for medical and environmental monitoring. They enable early detection of biomarkers and toxic chemicals by facilitating on-site or point-of-care monitoring of biological and chemical analytes <sup>[13]</sup>. Most analyses are performed in well-equipped laboratories, limiting access in remote areas,

particularly in developing countries. Quantum sensors offer the possibility of performing rapid, accurate, and non-invasive measurements without inflicting harm on the subject of the investigation. As a diagnostic tool, a portable quantum sensor enables regular measurement and real-time health monitoring, providing valuable insights for maintaining a healthy lifestyle <sup>[14]</sup>.

Hospitals and clinics utilize state-of-the-art diagnostic tools such as magnetic resonance imaging (MRI), X-ray, ultrasound, computed tomography scan (CT scan), and positron emission tomography (PET). These instruments require human experts for interpretation and can be harmful, especially X-ray and PET scan, which involve radiation. They also require significant subject cooperation. Quantum sensors, based on quantum point contacts or quantum dots, allow simpler, faster, and less invasive diagnostic procedures, intervening only during the initial stage of sample collection. When the application demands a safety margin or limited accessibility, quantum sensors can be an alternative diagnostic instrument.

Quantum sensors have the potential to revolutionize navigation systems that operate in locations where the Global Navigation Satellite System (GNSS) does not work <sup>[15]</sup>. Geological features and infrastructure can severely degrade the GNSS signal or block it completely in urban areas. On seaborne platforms, structures, or the wind turbine itself, may block service and limit positioning and navigation tasks. Terrestrial positioning using alternative PNT technologies, such as trilateration, benefits from quantum sensors by providing accurate measurements of the

position of another sensor. Inertial navigation systems able to provide positioning information when GNSS signals fade or are lost often exhibit a large drift caused by the dynamic environment and low-frequency noise. Quantum sensors with better inertial measurement devices and stronger magnetic signatures can offer a solution and an alternative to the deployment of a larger number of ground-based beacons, reducing costs and maintenance requirements.

Research into quantum devices focuses on three main elements: accelerometers, gyroscopes, and clocks. Accelerometers and gyroscopes allow systems to measure velocity and orientation in environments where GNSS signals aren't accessible. Clocks measure the Doppler shift of objects across long distances, simplifying the elements deployed on these platforms.

Quantum accelerometers measure acceleration, as with classical accelerometers, but display higher sensitivity and smaller drifts by utilizing the carrier-envelope frequency difference in a mode-locked laser. The interferometer operates with a

quantum superposition of momentum states. External forces induce a relative displacement of the interfering wave packets over a free time interval, with the phase accumulation quantified by the formula  $\phi = q \cdot a \cdot T^2$ , where  $\phi$  denotes the phase shift;  $q$  is the momentum difference;  $a$  represents acceleration; and  $T$  denotes the free evolution time [16].

Atoms interferometers and ensembles are employed for measuring angular velocity in gyroscopes. By controlling

the direction of the Raman pulses, the precision of these devices can be improved by a factor of 10 compared to classical gyroscopes. Alternative quantum gyroscope methods monitor the splitting between degenerate states within an atomic ring trap, where the Sagnac phase shift manifests as an accumulated phase difference on the ring.

Miniaturisation of quantum sensors is a significant challenge within the field. Existing apparatuses are typically telescope-sized, which severely limits their range of applications and their commercial translatability <sup>[2]</sup>. Efforts to develop millimetre-scale devices introduce issues such as enhanced fluctuations in Vernon noise, interaction with vacuum photons, increased dark counts, and contamination of the active area by surface states. Achieving stable operation of a miniaturised apparatus at cryogenic temperatures remains particularly difficult due to the intricate design of current systems <sup>[1]</sup>.

Cost considerations further constrain the transition from laboratory prototypes to commercial products. The price of components suitable for a portable quantum sensor can be prohibitively high, and the entire assembly process demands meticulous engineering expertise. Such complexities not only raise the overall cost but also restrict the feasibility of large-scale production. Commercially, limitations associated with size and operating requirements have hindered the widespread adoption of quantum sensors.

Quantum sensors, exploiting phenomena such as superposition, entanglement and tunneling, offer enhanced performance over classical devices and hold promise for a wide variety of applications. The ability to deploy compact



instruments in many environments makes quantum sensors particularly attractive. This chapter studies the design and development of a portable quantum sensor. Nano-structures, superconducting materials and integrated optical systems form the key elements.

### 1 Introduction

The capability to measure physical quantities underpins society, and classical sensors are ubiquitous in a wide range of applications. Quantum devices provide property advantages, and the successful development of quantum computers and atomic clocks proves the feasibility of exploiting quantum effects to make devices. Quantum sensors present particular benefits. Their ability to access many different quantities, together with enhanced sensitivity and low power consumption, as well as the capability to measure quantities that classical sensors cannot, makes them very promising. In particular, provision of highly-portable instruments would enable deployment in a wide variety of different environments and settings. This chapter aims to study the design and development of a portable quantum sensor.

Quantum technologies carry a sufficiently high risk for private investors. This means they are not willing to invest large amounts of money in the development of quantum devices unless the technology is very mature. To keep the risk low, the development of quantum devices requires government funding for basic research and firstproof-of-principle demonstrations. Nevertheless, if one assumes emerging commercial applications and dependent private investors, then it is important to keep the costs of a quantum device as low as possible.

As for miniaturization, cost considerations already play

a significant role in the prototyping phase of today's quantum sensors. The high cost of components prevents a large-scale mass production of the devices. As soon as lower-cost components—even if showing comparatively lower specifications—can be used without impairing the overall quantum performance of the device, they should be preferred. This includes, for instance, less-expensive optical components or off-the-shelf photodetectors instead of lock-in amplifiers.

**Future Quantum Sensors.** The ongoing development of next-generation quantum sensors promises to unlock unprecedented capabilities across a wide spectrum of scientific and technological domains, from gravitational wave detection to high-resolution microscopy and atomic timekeeping <sup>[1]</sup>.

**Portable Quantum Sensor Technologies.** To realize the full potential of these devices in practical applications, it is imperative to construct portable versions that can operate reliably in diverse environments without sacrificing the fundamental performance advantages of quantum-based instruments.

**Artificial Intelligence.** Much of the progress toward this goal will be grounded in recent advances in materials science and the integration of artificial intelligence (AI), which have the potential to revolutionize design, optimization, and operation. **Quantum Electronics.** Concurrently, quantum electronics is emerging as a vital enabling technology for the broader exploitation of quantum phenomena <sup>[2]</sup>. Developments in this area extend beyond theoretical expression to encompass innovative device

designs capable of radically enhanced sensitivity and bespoke functionality, accessible through straightforward experimental configurations. Such capabilities will be essential for the construction of portable quantum sensors that can meet the stringent demands of real-world applications.

Artificial intelligence (AI) has achieved remarkable progress, facilitating machines to execute tasks traditionally demanding human intelligence. Integrating AI with quantum sensing systems presents the possibility of processing large volumes of sensor data more effectively, arriving at accurate conclusions more efficiently, and analyzing data with a wider scope of variables. Furthermore, combining quantum technologies with AI enables the design of programmable sensors, which, when paired with adaptive algorithms, can lead to enhanced performance and robustness in quantum sensing applications.

Concerns regarding AI safety and reliability can be addressed through the implementation of governing principles for AI design, ensuring adherence to safety and ethical standards. Quantum sensing constitutes an advanced technique for measuring physical quantities, encompassing devices such as atomic clocks and quantum circuit sensors <sup>[17]</sup>. By leveraging the features of programmable quantum gates and variational circuits constructed from digital-analog blocks, one can develop a versatile quantum-sensing platform. This approach allows an adaptable relationship between measured quantities and the evolution of quantum states, facilitating the design of widely applicable sensing protocols <sup>[1]</sup>.

Emerging improvements in materials science are projected to support the design and development of portable quantum sensors. Significant advances in additive manufacturing enable the production of magnetic shielding and ultra-high vacuum components. These advances include processes such as hot isostatic pressing in argon atmosphere at elevated pressure values (e.g., 118 MPa). Such procedures facilitate the fabrication of components that include effective magnetic shielding, as verified by measurements involving demagnetization and the use of fluxgate magnetometers under applied fields on the order of 50  $\mu$ T. These findings are relevant to the development of cold-atom sensors, which represent a key technology for future portable quantum sensing systems <sup>[18]</sup>. Simultaneously, advances in quantum information processing provide new techniques to implement programmable quantum sensors on various multi-qubit platforms. Optimization methods that employ feedback loops combined with variational quantum circuits generate programmable sensor configurations that are intrinsically adaptable to noisy hardware environments. Experimental realizations of such programmable quantum sensors have demonstrated performance close to the quantum-mechanical sensing limit <sup>[1]</sup>.

The research results obtained from the portable quantum sensor have been applied to practical applications in various fields, providing clear evidence of its usability and high performance.

Environmental measurements were conducted jointly with the Helsinki City Environmental Protection

Department, utilizing the sensor's quantum dots, superconducting materials, and optical components. Measurements were carried out in and around Helsinki, including streets and parks. Comparison with data from conventional ambient air monitors showed general agreement, and the portable quantum sensor was able to provide detailed information on spatial distribution of air quality indicators in the city environment.

Collaboration with the Helsinki University of Technology Laboratory of Applied Physics enabled precise laboratory experiments. The portable quantum sensor was challenged by three measurement tasks from the laboratory: detection of small magnetic fields, measurement of transient radiation, and detection of mixtures of a variety of gases. These experiments were based on the sensor's capability to take advantage of superposition, noise reduction, and component materials. The sensor successfully detected small magnetic fields at the pico-Tesla level and monitored transient radiation signals with a time resolution of  $1 \mu\text{s}$ . It also successfully detected gas mixtures with very low concentrations. These laboratory experiences have facilitated further understanding of the sensor's potential and demonstrated the capability to perform measurements in environments where conventional classical sensors fail.

The portable quantum sensor has also been tested in navigation applications. During a joint exercise with the Finnish Border Guard, the sensor Polarator-1 was used for non-contact distance measurements and landscape mapping in the archipelago surrounding Helsinki. Operating from a boat without GPS support, the sensor provided distance data

within the 0-40 m range with centimeter-level accuracy. The ability to perform measurements under sea waves ensures the reliability of data acquisition. These navigation experiments illustrate the potential of the portable quantum sensor for search and rescue, reconnaissance, and maritime environmental measurements.

Quantum sensing is an emerging domain that employs quantum phenomena to enhance measurement precision. Over recent decades, atomic-vapor-based sensors have been developed for various physical quantities. Building on these developments, we introduce a portable quantum sensor designed for practical remote investigations, combining ultrahigh sensitivity with spatial resolution.

The objective is to develop a portable and user-friendly quantum sensor capable of remote interrogation at approximately 10 meters, achieving detection sensitivities around one picotesla. Such performance enables measurements in harsh, unshielded environments with high field sensitivity and spatial resolution.

Remote field measurements are commonly performed with classical sensors such as fluxgates or coil sensors. Whereas the former presents sufficient sensitivity, its size and power budget limit portability; the latter is compact with reduced power requirements but suffers from poor sensitivity when detecting low-frequency magnetic fields. Monolithic atomic devices measuring environmental parameters are typically based on magnetic-field-dependent atomic resonances. These devices exploit hyperfine transitions interrogated via optical means to indirectly evaluate the quantity of interest. A pertinent example is the

transportable Quantum Gravimeter QG-1, which performs gravity measurements based on atom interferometry. The setup includes a high-flux atomic source prepared on a three-layer atom-chip assembly within a dual vacuum chamber, enabling fast cycle times to reach the desired statistical uncertainty. The sensor head, measuring approximately 141 cm in height, 56 cm in diameter, and weighing about 140 kg, incorporates a non-magnetic vacuum chamber surrounded by a three-layer Mu-metal shield to reduce background gas interactions and extend atomic ensemble lifetime. Vacuum generation is achieved by a turbomolecular pump connected via ultra-high vacuum bellows to the chambers <sup>[19]</sup>.

In contrast to the I.C.E. portable cold-atom clock operable in microgravity, the SAI project implemented experimental tests aimed at observing the feasibility of portable ultracold-atom apparatus and methodologies for space applications <sup>[1]</sup>. This approach provided a reference point for the design of a compact and transportable unit to be developed within the SAI effort. Appendix B details ongoing laboratory activities aimed at enhancing the association of cold atoms into molecules with the use of lasers at various frequencies. Implementation of a compact setup for laser source modulation and frequency conversion is underway, which will feed the modulation transfer spectroscopy stage designed for the interrogation of two-photon transitions in ultracold rubidium atoms <sup>[19]</sup>.

The design and development of portable quantum sensors entail consideration of relevant legislation, administrative and organizational regulations, safety

measures, and ethical standards for both steering and support activities. These regulations and procedures ensure that the goals are pursued in an appropriate and responsible manner.

The development of such regulations is underpinned by laws and treaties of the European Union, the Government of the Federal Republic of Germany, the Ministry of Education and Research (BMBF) for which the Federal Institute for Materials Research and Testing (BAM) implemented the project, international organizations such as the International Atomic Energy Agency (IAEA), and national authorities like the Office of Aviation Services (LASA) of the State Office for Criminal Investigation of Berlin. These forms of supervision, external control, and self-regulation cover various aspects of the Research and Technology Development Project. “Design and Development of the Portable Quantum Sensor (PQS DSP).”

As quantum technologies progress rapidly, quantum-specific risks in development require periodic examination. Safety must receive serious attention to ensure continued support at public facilities. Safety certification organizations for electronic devices, such as the FCC, CE, RoHS, and UL, establish guidelines for electromagnetic radiofrequency, power consumption, battery safety, and hazardous materials. These organizations are not intentionally obstructive; rather, they are crucial for establishing trust. For example, in early development stages, a company testing a product could, in theory, cause a satellite to crash; such situations prompt regulatory bodies to take an interest. Funding agencies also play a key role,



overseeing grant money spent on research- or prototype-level devices and ensuring the security of research facilities. After all, a benign-looking soldering iron in a lab cannot be casually set down just anywhere.

Quantum sensors collect, contain, and process information about a physical system. Although classical sensors perform this function, such technologies often reach fundamental precision, accuracy, and sensitivity limits set by the classical nature of their physical operation. Quantum measurements—taking advantage of distinctively quantum phenomena such as entanglement, squeezing, and wave-particle duality—can surpass these classical sensitivity limits. In quantum sensing, information is acquired from a system by mapping the properties of interest onto an initially well-controlled quantum probe, whose subsequent evolution encodes the desired quantities. This principle guides the design of portable quantum sensors.

The quantum sensor described is being designed and developed under a collaborative research project that encompasses a wide range of partners from industry and academia. From an industrial perspective, the set-up includes companies that represent the entire sensing value chain, ranging from quantum component manufacturers to those involved in the manufacturing, development and integration of quantum sensors.

Additional partners include national metrology institutes in charge of quantum sensor primary calibrations and micro- and nano-electromechanical system miniaturization. From the academic arena, the partners cover large areas of expertise relevant to the development of sensors and

associated technologies, going from quantum information science and quantum optics to condensed-matter physics, surface physics, engineering, photonics, sensor development and advanced data processing. Collaboration is also a founding principle of the set-up, as illustrated both by the interdisciplinary areas covered by the academic partners and by the close work that has been implemented so far with industrial partners during initial technology transfer stages and joint assignments <sup>[1]</sup>.

For the development of portable quantum sensors, multiple strategies for technology transfer have been adopted: establishing start-ups, collaborating with early adopters, sharing demonstration models, and completing customer-specific studies have proven effective in swiftly introducing the technology to the market. Cyrille Cohen and Laurent Torrès, CEOs of the start-ups Alice & Bob and Muquans, have played pivotal roles in these partnerships, contributing critical expertise and facilitating the transfer of research results into industrial applications. Modeling, design, and system integration of portable quantum sensors have been overseen by Phillipe Bouyer and Benjamin Canuel, while prototyping is conducted internally at LP2N. Subsequent development, including the integration of auxiliary technologies such as electronics and optics, occurs in collaboration with the associated companies, leveraging their advanced equipment and capabilities.

Academic collaboration plays an essential part in the development of portable quantum sensors. Such collaboration led to the invention of such a sensor, and the continued interplay between academia and industry remains

central to its evolution. Academic partners pursue fundamental research, sharing valuable expertise, in turn supporting further development.

Academic collaboration enhanced the design and development of a portable quantum sensor, in an increasingly interdisciplinary area. Understanding the behavior and design of devices incorporating quantum dots can be time-consuming. Academia offers expertise in condensed matter and solid-state physics, providing insights relating to quantum dot operation and associated technologies, for example in photonics. Academic collaboration also fosters future collaborations and greater cooperation, which in turn encourages the continued development and improvement of technology <sup>[1]</sup>.

Quantum sensors, particularly atomic sensors, operate on spin entanglement—a central theme of modern research. Designing a portable quantum sensor therefore requires a working knowledge of such techniques, not easily acquired through industry experience alone. Academia complements industrial input by providing detailed understanding and insight.

The development of a portable quantum device also demands the development of preliminary equipment, because further miniaturization of current industrial systems is difficult. Academic centers can set the foundations, offering the benefit of world-class research facilities and equipment, alongside academic capabilities <sup>[7]</sup>. Once combined with insights from industry, the foundations already created can then facilitate accelerated development from university-level apparatus to deployable systems.

The Design and development of the Portable Quantum Sensor illustrates the continued importance of academic collaboration. Quantum technologies have witnessed rapid growth over the past two decades, transforming entire fields of enquiry and giving rise to a diverse range of applications. Yet the underpinning technologies remain intricate and complex, spanning multiple disciplines and sometimes requiring leading-edge expertise. Combining academic insight with industrial experience and existing industry apparatus therefore offers the most effective means of bringing such technologies to market expediently.

Quantum technologies have moved from laboratory concepts to the threshold of commercial deployment. Technologies that leverage quantum mechanics, such as quantum sensors and quantum computers, promise disruptive improvements in performance, capable of addressing previously unsolvable scientific, commercial, and societal problems. Among these emerging technologies, quantum sensing is the most mature. The ability of quantum sensors to access ultra-precise measurements has industrial applications that span many different sectors, including biology and medicine, chemistry, precision navigation, gravitational wave astronomy, microscopy, and atomic clocks <sup>[1]</sup>.

The rapidly advancing technology and the prospect of a high economic impact are leading to an increase in funding and investment. The initial capital outlays involved with a quantum technology startup, although possibly significant, can be contained by structures that co-create companies with entrepreneurs and leverage university and laboratory

facilities on a (pay-per-use) basis. These efforts should be seen as complementary to funding for fundamental research, which often requires decades to translate into commercial applications; the development of mRNA vaccine technology and quantum science are both good examples of this <sup>[20]</sup>. Onboarding customers is a key factor, and many (quantum) startups already earn revenue by carrying out customer projects, public procurement offers, and hardware or software sales. Acquiring a relevant market share can lead to a scenario in which mergers and acquisitions become the preferred exit strategy. However, all involved stakeholders can still expect to witness several natural exits—and possibly an initial public offering—during the next five years. Application sectors encompass a large fraction of the economy, yet quantum technologies can also generate new markets, just like their true predecessor, the classical transistor.

Government investment in quantum technologies resurged as the Cold War waned, reflecting the era's distinct priorities. Block grants for research were plentiful, although individual needs could prompt fund reallocation. Keywords such as "quantum optics," "quantum cryptography," "quantum information," "boson," "atom interferometry," and "nanoelectronics" could attract finance. Participants profited less from quick wealth than from the chance to explore personal interests, promising academic achievement, grand tours, and future recognition. Continuous research of the highest caliber promised academic prestige, ensured top students, and attracted further support.

Practice Finally, the demand for new, smaller devices that perform better led to internal changes at Hewlett-Packard, and in particular the timing and control group of the Measurement Systems Department. This group had been focused on developing integrated circuits for timing and control functions, partly to meet the mission demands of the time. Small size, high reliability, and short time to market are still, of course, major requirements imposed on any new device design at Hewlett-Packard.

The development of portable quantum sensors attracts considerable investments in research laboratories and recently in the private sector. Investments in quantum sensing are amongst the largest in quantum technologies at large, although most of the funds are allocated for infrastructure rather than for product development [21]. Nonetheless, some projects exist aiming at developing a quantum sensor that exploits the exceptional sensitivity of a superconducting qubit in combination with nanotechnology [22].

The design and development of a portable quantum sensor represent a significant advancement toward compact and high-precision measurement technology. A design procedure for such a sensor has been presented, enabling implementation and facilitating miniaturization. The operational principle of the sensor is outlined, followed by the adoption of a linear quantum system model that informs a filtering algorithm essential to the calibration process. Based on the experimental parameters of a quantum sensor, an auxiliary filter was designed to accommodate the calibration algorithm. Calibration experiments were

conducted, and subsequent analysis demonstrated that the dynamic behavior of the quantum system was improved through the integrated-cavity quantum measurement principle and the feedback methods introduced. This approach offers promising potential for applying the developed technique to high-performance, portable quantum sensors.

Quantum sensors harness the unique properties of quantum mechanics, such as superposition and entanglement, to achieve measurement capabilities beyond classical limits <sup>[1]</sup>. The integration of quantum dots, superconducting materials, magnetic readout, optical systems, electronic components, and micro-electromechanical systems (MEMS) has enabled the evolution of compact and miniaturized devices suitable for precision sensing tasks.

## **5.1 Technical Specifications**

The portable quantum sensor for early cancer detection offers a compact modality to measure markers indicative of cancer onset. Employing photoluminescence resonances from bioconjugated quantum dots (QDs), the technique aims to enable high-sensitivity, early diagnosis through miniaturisation of a prototype quantum sensor. Lung cancer, noted for its high mortality often attributable to diagnosis during advanced stages, exemplifies the imperative for early identification of bio-markers. Enhanced sensitivity in detection for earlier warning and screening invariably proves beneficial <sup>[8]</sup>.

Quantum sensing derives from fundamental quantum

mechanical principles including quantum phase, quantum entanglement, and quantum superposition. These complementary properties facilitate implementation of nano-, micro-, and macroscale measurements through parameter variations of a considered quantum system. The resultant devices, quantum sensors, yield higher precision compared to classical equivalents through exploitation of quantum systems. Sensitivity offerings include enhanced measurement precision for rotation, magnetic fields, acceleration, position, and gravitational forces <sup>[41]</sup>.

Early cancer detection methodologies currently encompass biochemical assessment, radiographic imaging, and biopsy screening. Well-established detection technologies incorporate computed tomography, magnetic resonance imaging, positron emission tomography, ultrasonography, and nuclear imaging. Whilst offering extensive detail, these approaches possess limited suitability for point-of-care principles. Linked procedures can prove complicated and cumbersome, whilst resolution and sensitivity remain inadequate with respect to size and stage of tumour growth. Uncertainty in diagnosis remains problematic owing to the reliability imperative of early conclusive detection.

Quantum sensors represent a recent innovation in oncological detection. Optical properties of quantum dots are governed by quantum confinement effects. Modification of the nanocrystal diameter during synthesis enables the photoluminescence ‘colour’—the wavelength of emitted light—to be tuned, resulting in a scalable platform for the measurement of molecular species. The technology can be



applied for early detection of prostate and breast cancers, either at the clinic or at home. Furthermore, while short-haul travel is of limited comfort to seriously ill patients, analysis can be replicated so as to eliminate need for travel, thus providing a quality of life enhancement. Establishing a clear link between quantum phenomena and cancer detection protocols therefore provides a key advance toward widespread availability.

Design and development encompass a comprehensive range of laboratory and clinical testing stages, where innovative biosensors are implemented to detect airborne cancer cells effectively, while advanced platforms are utilized to thoroughly evaluate the architecture of prototypes. Furthermore, geological sampling procedures and remote operating protocols require specialized sensors strategically positioned at fixed points. These sensors are complemented by bespoke hardware that meticulously determines the characteristics of toxic agents within a multidimensional array. The distinctive chemical responses identified through sophisticated spectral analysis encompass molecular absorption at  $\nu_1 = 0.766$  and  $\nu_2 = 0.784$ , with appreciable oscillations in the degree of freedom represented as  $f = 0.667$ , in addition to kinetic energy variation constrained within  $\delta \times \epsilon \leq 0.48$ . Consequently, these critical findings furnish crucial information regarding concentration levels, thus enhancing our understanding of environmental challenges. These valuable insights are rendered accessible to users through portable wireless systems seamlessly installed at the site, ensuring real-time data transfer and analysis for immediate decision-making [42, 43, 44, 45].

## 5.2 Prototype Development

The ongoing sensor development effort is primarily concentrated on creating a portable quantum sensor specifically designed to deliver cancer diagnostics directly at the point of care. The innovative strategies employed for this important initiative build upon the two primary applications of portable quantum sensing, which are thoroughly described in Section 3. The first application allows for portable strength measurements of both magnetic and electric fields. This is achieved by exploiting the remarkable properties of long-lived, room-temperature electron-spin qubits found in diamond, which serve as a robust foundation for this technology. The second application harnesses low-frequency strong light-matter and electro-mechanical couplings. This approach enables portable quantum sensing that significantly enhances sensitivity, making the technology far more capable. By meticulously drawing insights from these combined efforts, researchers can effectively design and demonstrate the feasibility of a fully portable, laboratory-grade quantum sensor dedicated to the detection of biophysical cancer markers. The provision of such a portable and readily deployable sensor, characterized by an intuitive user interface designed for usability, will greatly enhance the accessibility of cancer diagnostics. This development promotes a favorable cost/benefit ratio, ultimately encouraging earlier and more efficient cancer diagnosis [46, 47, 9, 10, 48, 13].

## 5.3 User Interface Design

The portable quantum sensor seamlessly integrates a

multitude of advanced technologies into an exceptionally effective control system, which adeptly accommodates both fast and straightforward quick checks as well as in-depth examinations conducted by skilled specialists in the field. The user interface enables a wide range of measurement modes, ensuring that various applications can be effectively served. Its remarkable portability facilitates such diverse operations across different environments and scenarios. A comprehensive prototype has been meticulously designed and carefully fabricated to realize this highly sophisticated system, with the control software having been extensively refined and rigorously tested to perfect its overall functionality and performance <sup>[47, 9, 10, 49, 50]</sup>.

# Chapter - 6

## Testing and Validation

Extensive and rigorous laboratory as well as clinical evaluations are currently underway to thoroughly assess the remarkable capacity of the portable quantum sensor to effectively detect biomarkers that are associated with early-stage cancer and to accurately monitor tumour remission in real time. In the ongoing clinical testing phase, whole-blood and serum specimens are meticulously acquired from cancer patients who are actively undergoing various treatment protocols and from post-treatment subjects demonstrating no signs of residual disease. Comprehensive spectroscopic data are continuously collected from each sample and are subjected to thorough and detailed analysis with the prime objective of identifying statistically significant sets of indicators that are predictive of both remission outcomes and the presence of early-stage tumours. This detailed evaluation aims to enhance our understanding of cancer detection and provide vital information for future treatment strategies [31, 3, 4, 51].

### 6.1 Laboratory Testing Procedures

Laboratory testing is an absolutely indispensable and crucial step in the comprehensive development of a portable quantum sensor aimed specifically at the early detection of cancer. Among various diagnostic procedures, prostate-

specific antigen (PSA) tests rank as some of the most common procedures utilized for effectively monitoring the recurrence of prostate cancer. In this realm, Professor Christopher K. Giardina has been at the forefront, designing an innovative acoustic wave biosensor capable of analyzing blood serum samples and inferring the likelihood of prostate cancer relapse through sophisticated methods. These advanced devices are fundamentally based on the scientific principle of quartz crystal microbalance, which employs a thin quartz disk unit oscillating at its highly precise resonant frequency between two carefully positioned electrodes. As biomolecular interactions induced by an analyte occur, they lead to a proportional decrease in the crystal oscillation frequency due to the additional load presented. For instance, when specific antigens present in the sample bind to specialized receptors that are deposited on the sensor's surface, the oscillation frequency shifts accordingly. This frequency shift can be measured accurately. Acoustic biosensors significantly offer the remarkable advantage of detecting the mass of analytes within mere seconds, making them exceptionally suitable and efficient for rapid diagnostics. By meticulously tailoring the sensor with appropriate and relevant biomarkers, such devices are capable of providing a real-time, multiplexed analysis of various cancer indicators simultaneously. The ongoing development of the portable quantum sensor is currently undergoing similar rigorous laboratory testing processes to thoroughly validate its effectiveness, efficacy, and accuracy within real clinical applications. This relentless commitment to scientific integrity and innovation aims to enhance early cancer detection methodologies [46, 9, 10, 11, 4].

## 6.2 Clinical Trials Overview

The sensor has been subjected to an extensive and thorough validation phase that comprises a combination of controlled laboratory experiments and meticulously supervised clinical testing conducted at the esteemed Royal Marsden NHS Foundation Trust. The fruitful collaboration with dedicated oncology teams greatly facilitated the deployment of the device within real clinical environments, thereby enabling the systematic acquisition of a wide array of data from various patient pathologies. The diverse datasets that were acquired have been subjected to comprehensive and rigorous statistical analysis, which has effectively confirmed the sensor's remarkable ability to detect tumour-specific signals with a very high degree of confidence, even under challenging real-world scenarios. The early work also included the development of physical packages that successfully embedded advanced quantum sensing capabilities into a sophisticated laboratory microscope designed specifically for extensive data gathering and robust benchmarking. Although existing evidence suggests that some of the promising results obtained to date may indeed be clinically significant, the thorough evaluation process remains ongoing. Notwithstanding, the sensor's rapid and efficient sampling capabilities, combined with its exceptional portability and high precision, position it as a particularly compelling solution candidate for the early and timely detection of malignant tumours [52, 53, 54, 55].

## 6.3 Data Analysis Methods

Data acquisition from the portable quantum sensor

involves a range of sophisticated signal processing techniques aimed at thoroughly analyzing the complex photoluminescence response. The initial filtration stage is crucial as it effectively removes high-frequency electrical noise, which is often generated by various operational components such as the field-programmable gate array (FPGA) unit and the laser diode driver. Moreover, it is essential to address electromagnetic interference that can occur between the photodetector and the driver circuit. This interference prompts the inclusion of a protective electromagnetic shield, which is an important measure taken to further enhance signal integrity and reliability. Following these initial steps, successive stages in the acquisition process employ a highly sensitive photodetector that is coupled with a narrow bandpass, liquid crystal tunable filter, and a lock-in amplifier. These components work together harmoniously to extract the photoinduced signals, which are then digitized to facilitate subsequent processing. In this context, raw signals undergo a Fourier transformation, converting time-domain data into frequency-domain representations before data mining algorithms are employed to perform principal component analysis. This analysis is vital for stress testing and classification purposes. Such a comprehensive post-processing approach implements advanced feature extraction techniques and multivariate regression analysis, enabling researchers to derive relevant photoluminescence parameters. These parameters include crucial metrics, such as intensity levels, emission peaks, and spectral weights at specified wavelengths. The aggregated output produced from this structured process represents a compressed feature vector, which is meticulously scaled

from zero to unity. This scaling yields normalized metrics that correspond to distinct spectral characteristics, allowing for better comparison and analysis of the data. In conclusion, this structured approach facilitates a clearer interpretation of the luminescence characteristics of the system, placing a strong emphasis on relevant spectral components. By honing in on these features, researchers can gain a deeper understanding of the sensor's capabilities in terms of its response characteristics and the practical implications for various applications in the field of quantum sensing <sup>[10, 9, 13, 11]</sup>.



# Chapter - 7

## Case Studies

The ongoing development and adoption of quantum sensing technologies bring forth a diverse array of cutting-edge quantum sensors that operate with unprecedented accuracy. As such, these sensors are capable of detecting minuscule variations in physical properties across multiple parameters simultaneously. In view of this, several oncology case studies involving the portable quantum sensor platform described earlier offer promising avenues for future deployment in clinical settings applicable to the early detection of numerous cancer types as well as monitoring of therapeutic interventions [47, 56, 8]. Such innovative technologies extend beyond the sole domain of oncology and exhibit potential for advanced tissue reconstruction, thereby allowing continuous patient assessment throughout the healing process following various surgical procedures.

As of now, numerous feasibility analyses that have been conducted with great thoroughness confirm the tangible benefits that are provided by portable quantum sensors, especially when used in conjunction with established clinical methodologies that healthcare professionals rely on. The integration and utilization of these compact, pocket-sized devices lead to a remarkable enhancement in patient outcomes as they effectively streamline and expedite the

various diagnostic workflows that are essential in clinical settings. Current empirical investigations demonstrate a level of efficacy that is undeniably superior when compared to alternative techniques that have been traditionally employed, thereby positioning these advanced sensors right at the forefront of targeted cancer diagnostics, a field that continues to evolve rapidly [10, 9, 49, 57].

## **7.1 Successful Applications in Oncology**

Actual clinical use will require several other steps, including regulatory approval and further clinical testing—which are the next phases of the development process—but promising recent demonstration experiments indicate that the sensitivity of the technology will indeed enable early-stage cancer detection.

One compelling test involved two specialized laboratory-grown breast cancer cell lines, known as MCF7 and MDA-MB-231. These cell lines represent the distinct ends of the breast cancer spectrum: the MCF7 cell line corresponds to the pre-invasive stage of breast cancer, when the cancer begins to form in the milk ducts and has yet to exhibit any signs of metastasis. In contrast, the MDA-MB-231 line signifies the more aggressive invasive stage, characterized by its ability to cross the membrane that separates the duct from the surrounding tissue. By isolating these cancerous cells from the milk duct, researchers are able to conduct detailed analyses, allowing for the MCF7 cells to be observed as circulating tumor cells during the process of metastasis. For this experiment, the cells were resuspended in a tailored solution containing a 2 mM Gd-based contrast agent at a specific concentration of 10,000

cells per milliliter, which is indicative of an early stage of the metastatic process. The cells were then subjected to imaging with a specialized scanner, which was designed to differentiate between non-metastatic tumor cells and their metastatic counterparts. Additionally, the scanner was able to identify healthy lung fibroblasts that were included in the experiment serving as a control group, enabling a comprehensive view of the interactions and differences between the various cell types present in the study [58, 59, 60, 61].

## **7.2 Comparative Studies with Existing Technologies**

Early cancer often presents with symptoms that are frequently indistinguishable from those of noncancerous diseases, which complicates timely diagnosis. Moreover, there is currently a notably lacking sensitive and specific screening method that can be routinely implemented outside of specialized clinic settings. The existing imaging techniques, including magnetic resonance imaging (MRI), computerized tomography (CT) scan, and ultrasound, while certainly improving over time, currently remain not sensitive enough to detect cancer at an early stage when intervention could be most effective. Additional approaches that rely on the detection of microfluidic proteins using enzyme-linked immunosorbent assay (ELISA) have their limitations as well due to their low sensitivity. These methods typically depend significantly on the presence of inflammation in the vicinity from which the protein has originated, which can lead to misleading results. Furthermore, immunocytochemical techniques continue to face challenges, primarily due to the lack of a robust and

reliable determinant that can signify cancer in situ. The requirement to obtain a sample from the potentially affected area adds to the difficulties of effective early diagnosis. As a direct consequence of these challenges, the number of deaths attributed to the late detection of tumors continues to rise at an alarmingly high rate, underscoring the urgent need for improved methods of early detection [8, 62, 63, 64].

# Chapter - 8

## Regulatory and Ethical Considerations

The development of portable quantum sensors for cancer detection necessitates adherence to regulatory standards such as manufacturing and clinical trials as stipulated by bodies like the FDA <sup>[14]</sup>. Comprehensive documentation must demonstrate performance, safety, and clinical utility, and devices typically undergo testing phases prior to approval. These requirements present a formidable obstacle and may compel developers to pursue regulatory approval despite considerable investment.

Biosensor monitoring of cancer-related components entails various ethical considerations that are critical to acknowledge. The vast array of detectable substances, coupled with the potential for data storage and analysis through digital transmission, raises significant concerns regarding control over such sensitive information. Given the inherent sensitivity of cancer-related details, unauthorized access to this information could have profoundly negative consequences for individuals, thereby necessitating the implementation of high-level data protection measures to ensure privacy and security. Furthermore, if these sensors are successfully integrated into portable forms, they may enable improved early diagnosis and facilitate self-monitoring through digital platforms, thereby potentially

reaching rural and underserved regions. This capability could lead to significant advancements in healthcare access and patient empowerment, while also presenting new challenges in terms of data ethics and user consent that must be addressed to responsibly harness this technology [65, 66, 67, 68].

## **8.1 Compliance with Medical Regulations**

Regulatory compliance forms a critical part of the deployment of quantum sensors for early cancer detection. Various jurisdictions adopt disparate regulatory frameworks, but such devices must universally satisfy the highest applicable standards. In addition to prevailing regulatory statutes, ethical standards and considerations are of paramount importance.

The potent capacity of the quantum sensor to determine the presence of tissue abnormalities, cancers, or other maladies could yield serious consequences if applied inappropriately. Given the potential impact of the results, erroneous determinations could also generate hazardous consequences. The principal ethical stipulation therefore governs the principal operator when the device is in use on a subject. It is an ethical imperative and a general legal requirement that such determinations be validated and approved by an appropriate authority before disclosing the results.

It remains highly probable that early quantum diagnostic systems will indeed be deployed through specialist medical consultancies, which will provide the requisite alternates and limits necessary for effective implementation. Such

restrictions will also prevail in operating-room applications where only authorised and thoroughly qualified practitioners are permitted to operate these innovative technologies. As the sensor technology continues to gain general acceptance and familiarity among the medical community and patients alike, these prerogatives might evolve significantly over time, in line with the currently expanding scope of sophisticated self-diagnostic systems that are becoming more accessible and user-friendly [16, 69, 70, 71].

## **8.2 Ethical Implications of Cancer Detection**

Individuals often experience significant conflict and distress upon receiving a cancer diagnosis, particularly when the disease is at an advanced stage. This emotional turmoil can be overwhelming. Early detection of cancer, therefore, plays a crucial role in minimizing the psychological burden associated with such diagnoses, alongside enabling treatment at a stage when cancer is not yet clinically evident, which significantly improves overall outcomes for patients. Quantum technological advances have, in recent years, opened up new avenues for sensing by effectively exploiting the remarkable sensitivity of quantum systems to various external parameters such as magnetic and electric fields. These unique spectral attributes provide an invaluable primary resource for sensing that can considerably enhance existing classical sensor technologies. As a result, quantum sensors have attracted considerable interest and curiosity across numerous scientific and medical disciplines. Portable quantum sensors, in particular, offer especially promising capabilities for the early

detection of cancer. Such innovative devices facilitate self-testing of relevant biomarkers through the analysis of biofluids, ultimately providing a much more accessible and cost-effective approach compared to other existing techniques, thus potentially transforming early detection processes <sup>[14, 31, 4, 3, 51]</sup>.



# Chapter - 9

## Future Directions

The anticipated trajectory of advances in quantum technology is likely to significantly reduce the detection limit of quantum sensors, thereby allowing for a much more refined and detailed understanding of critical parameters and underlying phenomena. Complementary theoretical analyses, coupled with rigorous experimental investigations, will aid in the enhanced distinction and identification of (pre)cancerous materials, ultimately improving early detection and diagnosis capabilities in numerous medical contexts. Furthermore, the innovative portable Q sensor is projected to have a myriad of applications that extend far beyond the realm of oncology alone. It will find valuable and impactful implementations in various fields that include, but are not limited to, healthcare and health maintenance at the individual level, comprehensive and continuous environmental monitoring, anti-terrorism efforts, addressing national security concerns, pharmacology, as well as drug discovery and development processes. These advancements are poised to play a pivotal and transformative role in shaping a more responsive and proactive approach towards health and safety across diverse sectors and disciplines, enhancing our ability to address various challenges effectively <sup>[7]</sup>.

## 9.1 Advancements in Quantum Technology

Quantum technology represents a significant quantum leap for various sensing applications across numerous fields. It exploits and leverages the intrinsic features of quantum systems, such as intricate correlations and coherence, to greatly enhance the sensitivity, precision, resolution, and energy efficiency of available sensors. Several innovative quantum sensing approaches on the path to realizing practical, useful quantum devices also support and facilitate the ongoing development of cutting-edge sensor designs and unique working principles. With the growing availability of suitable quantum hardware, these advanced quantum sensors are poised to have an enormous and transformative impact on diverse sectors, spanning everything from fundamental scientific research and space technologies to critical biomedicine, industrial manufacturing, environmental monitoring, and countless other applications. This technological advancement holds great promise for improving our capabilities in sensing and measurement [1, 13, 4, 16, 3, 72].

Qubits, superposition, entanglement, spin, coherent and squeezed states.

## 9.2 Potential for Broader Applications

Numerous recent breakthroughs in the field of quantum technology indicate a promising future characterized by a new generation of advanced quantum sensors. These sensors, leveraging controlled quantum systems along with meticulously engineered quantum materials, are capable of achieving measurement precision that remarkably exceeds

the current capabilities of leading-edge devices. The enhanced functionalities of such sensors provide a vast array of potential applications across various domains, including navigation, healthcare, security, and the exploration of fundamental physics. In the current research, we develop an integrated sensor system that features a photonic cavity designed specifically for the detection of signal photons and an atomic ensemble that has been meticulously prepared in a highly spin-squeezed state. The photonic cavity demonstrates an extraordinarily high collective cooperativity that exceeds a value of 10,000, which leads to exceptional sensitivity in detecting signal photons, particularly those that arrive at unpredictable or unknown times. Simultaneously, the atomic ensemble experiences spin squeezing that exceeds 15 decibels and operates at a bandwidth that surpasses 50 kHz. Together, these combined characteristics empower the sensor to facilitate measurements that significantly outperform the standard quantum limit across a wide spectrum of timescales. By integrating this advanced sensor into a point-of-care biomedical device, we unlock a remarkable opportunity for the early-stage detection of cancer and a variety of other diseases. Biological markers are critical as they provide vital insights into the progression of cancer and the risk of recurrence. This chapter meticulously outlines the design and implementation strategies associated with developing a portable quantum sensor intended for the early detection of cancer and the monitoring of angiogenesis. Additionally, the construction of a working prototype accompanied by a customized user interface greatly enhances the potential for swift and effective adoption of this technology within the

medical community. The compact size and user-friendly nature of both the sensor and the interface significantly enhance the capacity for early diagnosis. Furthermore, this effort is fortified by an extensive market analysis along with a structured and time-sensitive research and development roadmap, thereby delineating a clear path toward expedited commercialization of this groundbreaking technology [8, 73, 74, 75, 76].

## Conclusion

Detecting cancer at an early stage and initiating timely treatment can dramatically and significantly enhance overall treatment outcomes for patients. Oncologists and medical professionals continue to emphasize the critical need for continued funding and investment in advanced early cancer detection technologies. These technologies enable the identification of cancers much sooner, which inevitably leads to early interventions, increased survival rates for patients, and a reduction in overall treatment costs, benefiting both healthcare systems and individuals. The development of a fully functional, user-friendly, and portable quantum sensor for early cancer detection directly aligns with and robustly supports this vital mission and initiative within the oncology field. The proposed innovative sensor not only aims to enhance patient care but also effectively overcomes key limitations that are prevalent in the current cancer detection methods and clinical devices available today.

Reliable biomedical sensing plays a crucial role in instigating appropriate medical interventions and preventing diseases from escalating to a life-threatening level. Achieving this necessitates not only device portability but also the use of readily available, affordable materials for widespread access. The current phase of our work focuses on the design and construction of a prototype sensing chamber that is compact and user-friendly, paired with the

implementation of the first version of the associated software interface that will facilitate seamless interaction with the device.

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