American Journal of Botany and Bioengineering
https://biojournals.us/index.php/AJBB
ISSN: 2997-9331

Quantum Imaging in Medical Diagnostics: The Future of Non-Invasive Precision Medicine

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Received: 2025 19, Mar
Accepted: 2025 28, Apr
Published: 2025 31, May

Annotation: Medical imaging plays a crucial role in diagnostics, guiding both invasive and non-invasive medical procedures. Since the invention of the X-ray method in 1895, numerous medical imaging techniques have been developed, including widely used technologies like CT, MRI, ultrasound, and PET scans. Contemporary medical imaging relies heavily on electromagnetic radiation in the range of 10^−14−10^−1 m, which carries information about structures and phenomena in the human body. Quantum technologies, particularly quantum-enhanced imaging techniques, can improve the state-of-the-art performance of a few sub-technologies of MRI tailored for medical applications.

In recent years, the number of publications on quantum imaging, sensing, and metrology has increased significantly, demonstrating the high interest in this research area and the applications prepared in different fields. The emergence of quantum imaging technology holds promises for various applications, bringing advanced techniques for imaging improvement and patient safety. Traditional imaging techniques encounter a resolution limit of the involved light, making it impossible for the imaging devices to utilize the light sub-wavelength. The performance of non-invasive imaging using nurse diagnosis is limited due to the sophistic frequencies of heart and lung sounds employed.

Proper spectral analysis techniques can be used to detect the respiratory rhythm of adults of various ages, frequency and transesophageal cardiac cycles, and global brain oscillations of elderly patients. Quantum optics enters another level on top of these classical optical techniques. Using entangled photons for imaging has obvious advantages as entanglement is known for connectivity. Health outcomes can be improved through quantum-enhanced medical imaging for non-invasive precision medicine.

1. Introduction to Quantum Imaging

Medical diagnostics has evolved considerably owing to multiple modalities of imaging techniques. From X-ray imaging to MRI and from CT scans to Doppler Ultrasound Imaging, a range of imaging technologies has been devised that have been gaining more popularity over the years. Yet, with this extensive technological outlook, limitations in achieving high-resolution images and the risk of potential harm to the human body are present, sparking interest in utilizing an entirely different aspect of science, quantum physics, to devise enhanced medical diagnostics and imaging tools [1]. Quantum imaging is foreseen to play a part in the future of non-invasive precision medicine.

Imagery quantum enhancement techniques find their application when to the limitations of the conventional capabilities of imaging modalities. Loss of insights into brain tissues or cardiac structures due to low resolution is one of the problems. The engendering of quantum entanglement to encode information about the observation has addressed this issue to provide a significant improvement in resolution over elastic scattering or fluorescence dual-photon imaging. Even though, unlike MRI instrumentation, imagery quantum enhancements techniques operate through the collaboration of quantum entanglement, a benefit of this is compatibility with the conventional imaging framework.

Another form of awareness that is not exploitable by conventional algorithms renders the echoes of different modalities insurmountable, such as smooth images from a fast-moving structure in Doppler Ultrasound Imaging or copper from complex background chemical compounds in Optical Imaging. Such issues arise in medical diagnostics and imaging for the human medical field, as well as for animals of zoo adventure parks, spas, and farms breeding. The necessity for better and smarter technologies is everywhere. Reasoning the issue by each modality by a tailored agent, there are trials to desire prescience focusing on pixels as conventional techniques, which yet ignored the subtle nature of the information in the featured states. Quantum Imaging is expected to be the solution for the most difficult but uncomplicated future of non-invasive precision medicine. [2][3][4]

2. The Basics of Quantum Mechanics

In 1900, Max Planck modeled the “black body” as a collection of oscillators and used the empirical formula for the average energy of an oscillator to derive the black body formula. In a classical approach, an oscillator would have an energy distribution that could be computed for each oscillator. In light of this derivation, it became clear that electromagnetic oscillators cannot take arbitrary energy values, but they exist in energy packets called “quanta”, whose energy is quantized in multiples of hf. This assumption was dubbed the idea of quantization and Planck became the father of modern physics. However, despite the success of the model, the most troubling aspect remained the idea of quantization of electromagnetic energy. It was only in 1905 when Einstein proposed the light quantum idea. Although it became fashionable to think of light as an electromagnetic wave and a collection of particles, photons, both approaches endowed light with a wave-particle duality which is characteristic for the entire quantum world and has no classical counterpart.

In 1927, Werner Heisenberg formulated his uncertainty relation which established that for observables x and p the largest precision in the simultaneously definable standard deviations is limited by a nonzero constant. The recognition of the wave-like nature of matter and the necessity of a statistical interpretation of the wave function in the Markov limit induced major probabilistic concepts in physics. Harold Urey and G.M. Lattes were among the first to attempt to apply the probabilistic approach to particle detection. However, both were soon faced with an insuperable difficulty: it was impossible to configure detector systems without disturbing the state of the incoming particles. Hence, new concepts had to be formulated to describe a coherent measurement where both the observer and the system being observed were treated on the same footing.

A solution was found only after some decades by John von Neumann and David Bohm who constructed alternative formulations of quantum mechanics. Experiments concerning Bell's theorem and the detection of quantum entanglement provided strong evidence in favor of quantum predictions over its classical hidden variable alternative. The probabilistic description of quantum realities paved the architectural ground for a new branch of understanding in both physics and technology: Quantum Information. Quantum perpendicular devices based on no-cloning, concurrent error correcting codes or quantum nonlocality have been envisaged and either constructed or realized in proof-of-principle schemes. [5][6][7]

3. Principles of Quantum Imaging Techniques

Quantum imaging deals with the possibility of realizing imaging procedures exploiting the peculiar properties of single quantum correlated states, with specific emphasis on imaging in the sub shot noise regime. The basics of quantum imaging will be illustrated starting from its classical understanding. The main two-particle, two-mode quantum correlated sources will be introduced. The main quantum imaging procedures will be described and the noiseless imaging and the quantum ghost imaging schemes will be discussed in detail. Finally, the experimental realizations of such techniques will be reviewed and the challenges and possible new directions will be pointed out [8].

The first techniques of imaging with quantum states of light were proposed at the beginning of the 1990s. The SAT technique exploits the sub shot noise correlations among two fields emitted by a non degenerate phase sensitive parametric amplifier. The noiseless image of the bright part of the object may be reconstructed only if both fields have reached an appropriate level of squeezing (i.e. variance of the amplitude fluctuations below 1/2). After the first proof of principle realizations, exploiting this technique, a complete reconstruction of the image was performed. The quantum ghost imaging uses two intensities-correlated fields, such as twin beams coming from a down conversion source, to obtain images of an object. A single image of the bright part of the object is obtained by comparing the measurement outcomes obtained using an intensity detector in one mode with those obtained using a time-resolved intensity detector in the other mode. The analysis of the outcomes is performed using a classical algorithm in the same spirit as for the usual imaging. Ghost imaging had its first proof of principle realization in 1995 and has developed with a large variety of techniques and kind of objects addressed. In the last decade, an increasing interest in the field of quantum imaging has been expressed by experimentalists with a strong wave of new results and original proposals, some of which implement original detection strategies.

3.1. Quantum Entanglement

Quantum entanglement refers to a distinctive quantum effect involving two or more distant particles. Traditionally, each distant particle in a system described by mathematical variables can be considered separately. For example, an ideal classical two-particle imaging system operated in the threshold detection limit uses a laser beam as the light source. A two-pixel imaging device retrieves the amplitude image, which is the product of the two image functions and the two pixel functions. However, in a maximally entangled two-particle system, the mathematical variables of the system can be split into two distinct sets. One is associated with one particle, while the other is associated with the second particle. A break of separability occurs. The local measurement of one particle in one pixel is completely independent of the measurement of the second particle in a later pixel. In this case, neither image function nor a single-pixel measurement can retrieve the original image; in other words, if either particle is independently detected, no information about the image can be obtained. Nevertheless, this system still preserves the coincidence measurement. For a time-bin entangled two-photon pair generated by spontaneous parametric down-conversion, there exists an EPR correlation in the time delay between the two photons [9]. Remembering that a local measurement can be used to control the measurement outcome of a distant system, this system is effectively no longer separable. The above correlated two-photon system has been used to demonstrate quantum imaging. Unlike classical imaging, the correlation between the two can be uniquely determined if one of the two particles is measured in the joint position-momentum basis. Also, due to the nonlocal EPR correlation, quantum imaging experiments can be done on an optically opaque object. In simple terms, the term “quantum imaging” refers to a piece of work that equivalently applies quantum mechanics in an imaging system and produces an image correlatively from measuring the quantum properties of photons illuminately either together with it or after it. Quantum entanglement seems more or less mysterious from a purely classical perspective. However, it has already started to play important roles in practical engineering applications [10]. With the rapid development of quantum optics and photonic technology, quantum imaging has gained more and more insight, especially in quantum biology, unexplained features in biophysics, and fascinating approaches beyond current classical techniques.

3.2. Quantum Superposition

In 2017, a sub-shot-noise wide field microscope based on non-classical photons number correlations in twin beams that produces real-time images of 8000 pixels at full resolution was presented. This system was found suitable for absorption imaging of complex structures due to a noise detection reduced to 80% of the shot noise level. In principle, this system can be further improved by a post-elaboration quantum enhanced median filter that returns a noise at around 30% : at trade-off with sensitivity for the best resolution achievable absorption microscopy [11].

Quantum superposition has been manipulated in a “quantum amplifier” to enhance the sensing capabilities in photonic applications. Quantum phase imaging can provide a wide field of view, non-contact method with high sensitivity and resolution to reveal morphological changes in cellular environments. This was used by developing a super-sensitive phase imager with space-polarization hyper-entanglement that operates over a large field-of-view without a scanning operation. Moreover, using this hyper-entanglement, imaging of 2330 µm × 2330 µm size protein microarray was carried out in a quantum-enhanced manner and fidelity enhancement through the scanning operation was reported [12].

It may be noted that passive phase imaging systems rely on rotatory polarization devices/filters to enhance the SNR and as such are limited by their sensitivity and acquisition speed. Quantum core devices exploit conditional measurements that either enhance the SNR and detect phase latencies, this mechanism usually requires a higher optical setup configuration due to sophisticated entangled sources. Additional device complexity and challenges in application implementation, e.g. adaptation for shaping wavefronts in massive arrays, severely limits their dissemination in the biomedical field.

4. Current Applications in Medical Diagnostics

In the medical field, quantum-enhanced imaging technologies are powerful tools that have the potential to rewrite the story of medical diagnostics and imaging. To bring about a next-gen medical imaging era of better resolution and improved contrast, quantum entanglement has been a recent breakthrough in the realm of medical imaging. The convergence of quantum mechanics and medical imaging is poised to elevate the quality of diagnoses and uncover hidden details of the workings of the human body. Applications of quantum sensing and imaging have been studied in many fields of medicine [1].

In neurology, quantum sensors, capable of detecting minute shifts in brain activity, hold promise for novel ways to diagnose and track the progression of neurological disorders. Engineering advances allow the study of models of Alzheimer's Disease to discover early biomarkers and develop novel therapies. Quantum dots have been successful in seeking out and imaging beta-amyloid plaques in diseased neural tissue. Diamond-based quantum sensors have been assessed toward studying and imaging neural patterns in the context of untreated and treated models of Parkinson's Disease. These applications provide compelling motivation for new methods for imaging brain processes that can exploit the principles of quantum mechanics.

Real-world applications of quantum sensing and imaging have yielded success in marginalizing noise in signal detection. In neurology, quantum sensors have been demonstrated to detect biomarkers for Alzheimer's disease that exceed the detection capability of standard techniques. Novel techniques, based on improved optical elucidation of quantum-enhanced images, provide the prospect of making atomic-scale cardiac structures and deviations visible with macro-scale medical devices able to be deployed in clinics. With improving proof-of-concept studies and ongoing exploration of clinical applicability, quantum sensors and imagers may soon grace the walls of hospitals. Building on this foundation, some limitations in the effectiveness of quantum imaging and sensing for medical purposes must be addressed if these novel techniques are to be clinical tools. [13][14][15]

4.1. Magnetic Resonance Imaging (MRI)

MRI is a versatile imaging technique that has undergone rapid development in the last years, transitioning from a technical approach to clinical practice. The ability of MRI to collect more information about a certain tissue than solely image intensity has raised great interest in biomarker development. Particularly MR fingerprinting (MRF) showed great promise and improved MRF acquisitions using signal modeling improved recovery of continuous relaxation distributions. Outside the brain there has been increasing interest in MRF approaches for the abdomen, meaning further increase in potential application areas for quantitative MRI [16].

Over the last years, MRI has established itself as a versatile imaging technique that is widely used in clinical practice. The ability of MRI to generate high-resolution images with an unmatched soft-tissue contrast has not only allowed for incredible insights into the morphology and structural integrity of the human body but also enabled access to a plethora of functional information regarding physiological processes [17]. However, despite their great diagnostic value, current standard techniques for quantitative imaging such as T1, T2, and diffusion tensor mapping face several challenges including long scan times and/or limited spatial resolution. Therefore, a plethora of methods have been designed to alleviate the burden of long scan times, by means of novel k-space sampling schemes including undersampled k-space data acquisitions, compressed sensing, deep learning based reconstructions, and a combination thereof. Over the last decade and gaining momentum in the last years, MRF has emerged as a unique and efficient framework for the acquisition and simultaneous estimations of multiple tissue properties in a single fast MR acquisition. State of the art research in the field has witnessed remarkable developments concerning the pulse sequence structure and parameter optimization, the reconstruction, and all subsequent investigation steps toward clinical usage.

4.2. Positron Emission Tomography (PET)

Positron Emission Tomography (PET) can measure tissue physiology with high sensitivity but lacks spatial resolution in the mm range needed to localise tumours or brain function. Novel engineering to exploit the quantum nature of positron annihilation photon pairs is being researched. A simulation of a Paxman Detector comprising a planar array of single-photon avalanche diodes with a laser validated the detection of quantum entanglement in the MeV regime and showed potential for further imaging improvements . In addition to the better characterisation of the spatially-resolved PSF from optics modelling, simulations successfully predicted the use of quantum entanglement in MeV photon Cherenkov pair production. The observation of entanglement and application in photon pairs from a Na22 source is an ongoing project. A proof-of-concept implementation of a QE-PET system is proposed.

Imaging research into the next generation of positron emission tomography (PET) is pushed by a growing need for cancer detection, diagnosis and therapy planning. The rapid rates of development of new drug therapies, such as monoclonal antibodies for both diagnosis and treatment of cancer, are creating opportunities for the pharmaceutical industry to develop alternatives to current single photon and PET approaches. Amongst those under consideration are completely new classes of detectors that exploit advances in nanotechnology [18]. However, the existing dynamic range and sensitivity of tomographic PET systems operating in the 511 keV energy regime remain unmatched. As the cancer incidence increases, there is also a need to provide the current standards of care to a larger population, largely in the developing world where the perfect technology may not be the same as that in the developed world. Until now efforts have aimed at developing systems based on traditional detector technologies to exploit the isotopes available for radiopharmaceutical production in a low cost approach. Nevertheless, since 2004 the situation has substantially improved with new potential isotopes targeted in existing cascades falling out of research reactors. However, such isotopes have significantly different beta+ decay profiles, which complicates the current down-scatter based approaches to developing new detectors. Although a number of possible future scintillation detectors are likely to satisfy the requirements of high-containment systems in the 511 keV regime, they are unlikely to be competitive in the broader arena of biomedical research.

4.3. Computed Tomography (CT)

Computed tomography (CT) was one of the first areas where significant results have been achieved in quantum imaging applications. With the onset of this century, attentions have turned to the prospects of utilizing quantum mechanical effects for CT applications. In this context, a broad variety of related quantum imaging applications literally revolutionize the imaging technology in many energy fields. This represents an entirely new area of research where optics need to play a significant role as well. Quantum wide-field microscopic imaging, quantum holography, quantum 3D imaging utilizing quantum entangled photons and ballistic missile detection via vacuum coherence imaging are a few promising outcomes and leads to the development of a novel generation of imaging systems, with higher sensitivity, lower noise, larger dynamic range and spatial resolution. The traditional CT image reconstructions assume that projections are available at a set of directions that is sufficient to satisfy the so-called uniqueness theorem. The most common techniques for this imaging modality are analytic reconstruction methods and numerical techniques. Energy-resolving detectors offer the ability to separate events by their energy. A quantum imaging encoder takes n bits and creates a single encoded photon. It is a nonlinear process and can only be done using a combination of nonlinear and linear optics.

The entanglement at a quantum level was utilized and successfully implemented in conjunction with detectors with time-resolve and energy-resolve capability. Using the predictive power of quantum theory, 4D CT is then considered for image reconstruction. CT is one of the most popular biomedical imaging modalities for non-invasively and safely obtaining high-resolution tomographic images. The result of a quantum algebraic reconstruction technique that uses a compressed qubit-encoded projection dataset to recover a continuous classical image from projected measurements. The instability of the compressed quantum projection dataset under noise suggests that quantum imaging applications should showcase the protocol until sufficiently mature techniques for mitigating noise are integrated into the proposed quantum approach. One of the pioneering works in quantum imaging is to encode spatial information of an image into photon's frequency. This researcher has studied to physically manipulate the spatial frequency of a beam and provided an experimental setup aiming to demonstrate quantum encoding image years ago. The original equal frequency beam has a broad frequency spectrum while reconstructed images have narrow frequency beam widths with halos around it. Other quantum imaging applications include quantum ghost imaging that uses time-reversed entangled photon pairs, quantum illumination that utilizes entangled light to image a single target buried in thermal noise environment. [19][20][21]

5. Advantages of Quantum Imaging Over Classical Methods

In the early 1970s, light-matter interactions were recognized as information carriers. This led to various imaging techniques that related the light emitted from an object to its spatial characteristics, such as photo-acoustic and fluorescence imaging. In all of these techniques, one common aspect is that light is the carrier of information and it is detected by means of a sensor. The information that is recorded by a sensor can be viewed as the output at the terminals of a photonic device (for instance, a lens). Thus, the data-acquisition process can be regarded as a linear transduction process, realizing an input-output behavior. This has facilitated the application of optical imaging techniques across a broad range of disciplines. Within each of these fields, there is relentless pursuit of techniques to increase the image resolution or contrast qualitatively and/or quantitatively.

Quantum optics, which deals with the quantum properties of light and its interactions with matter, has investigated imaging arrangements in which the illuminating/recording light field is affected by quantum mechanical uncertainties. In contrast to a classical uncorrelated light field, the quantum field can either improve the image quality of simple scenarios, or reveal behavior that cannot be understood within classical theories for more complex scenarios. These objects typically emit radiation fields that are described by classical wave functions with fixed amplitudes, phases and propagation directions. Impressed by the remarkable quantum effects routinely observed in mesoscopic systems, attention shifted to geometrically complicated systems of colossal size that are well described by classical physics.

There are several examples of imaging that can classically be treated in the geometric optics limit. Non-uniform scenarios were first cast into the quantum regime by incorporating the effects of spontaneous emission in lens imaging systems. The wave nature of light is the cause of great difficulties in achieving high resolution and image contrast. Adaptive optics is one of the techniques used to reduce the image degradation caused by the turbulent atmosphere. The images obtained by adaptive optics systems are classic. Beyond this technique, quantum entanglement has much more drastic advantages [22] [12].

5.1. Higher Resolution

Many high-resolution optical imaging modalities yield a certain degree of phase and amplitude variation of the incident wavefront recorded by a camera sensor. Quantitative phase imaging techniques estimate such variations to produce image contrast mechanisms not present in traditional amplitude imaging techniques. For instance, interference-based quantitative phase imaging techniques map optical path differences within the object, while spatial-light-modulator multiplexed quantitative phase imaging techniques recover the complex amplitude of the recorded field at the camera sensor. However, any quantitative phase imaging technique based on classical optics has its own inherent trade-off between field-of view and resolution dictated by the diffraction limit of visible light. This means that improved resolution capability usually results in significantly reduced accessible sample area, leading to a potential loss of information. Moreover, given the demand for pre-clinical and clinical biomedical diagnosis and therapeutics, there is an increasing need for wide-field, high-resolution imaging at low-cost platforms to ensure affordability.

Quantum optical technologies have the potential to introduce superior imaging capabilities over their classical counterparts. Some of the strategies proposed to this aim exploit quantum-noise-free imaging techniques to improve sensitivity, resolution, or both. These benefits include quantum-enhanced imaging with squeezed light, quantum-image processing, quantum-enhanced imaging with super-resolving techniques, and quantum illumination using entangled-photons. Nonetheless, all these strategies demand highly complex optical setups; they are typically limited to single-pixel imaging formats and require specialized components for practical implementation.

Currently, a quantum-entangled four-photon hyperspectral state generator that operates at non-cryogenic temperatures compatible with ensemble-scale integration in silicon is presented. Quantum hyper-spectral imaging and Raman spectroscopy techniques using the four-photon tensor product state are developed. After successfully demonstrating cryogenic-compatible silicon-based four-photon sources and quantum frequency interference techniques, the microstructured four-photon dispersion phase-matching sources could be an alternative compact platform for quantum-technology applications in the mid-infrared. [23]

5.2. Increased Sensitivity

Quantum sensors exploit quantum effects such as superposition or entanglement to achieve superior performance, for example, in better measurements of time, energy, magnetic fields, or other physical observables and parameters. Many quantum sensing applications have been realized by different types of quantum sensors, from ground-based to space-based. Quantum sensors can also be portable (ideally) or even wearable, making them a kind of ubiquitous sensor for mobile platforms and various biomedical applications [24].

A promise of improving the sensitivity of quantum sensors comes from the non-classical nature of quantum measurement. For example, instead of using coherent state light from a laser, researchers can use squeezed light for measurement-enhanced detection of optical signals, yielding extra phase shifts for optical sensors. Another class of quantum-enhanced sensors employs quantum entangled photon pairs, which are produced by spontaneous parametric down conversion or four-wave mixing processes for the metrology of various observables, such as time-frequency photons, spatial resolution, optical phase detection, and polarimetric measurements. For example, with either polarization-entangled or time-bin entangled photon pairs, quantum-enhanced imaging techniques have been demonstrated and theoretically well founded [12].

5.3. Reduced Radiation Exposure

Since the advent of coefficients of variation for quantum noise to attain the desired image quality, efforts have been made to emulate a lower dose with a lower mA X-ray source and a higher quantum efficiency (QE) detector. A phantom study with a low dose X-ray imaging (LDXI) prototype showed maximum target-to-target images resolution of 605 microns for female, 870 microns for male, and 484 microns for mixed gender standard resolution cohort. The DDSs of the lowest pixel sizes at 1.8 MHz bandwidth white Gaussian noise were considerably same for 392 mA for the current and 63 mA for the LDXI, being 18.3 and 17.7, respectively. Reduced ToDs and pixel sizes achieved under a lower mA X-ray excitation source at a better maximum diagnostic image resolution and similar temporal resolution were reported for better radiotherapy achievement [25].

Dose savings in CT are generally a function of scan mode, computer software development, and hardware changes. Quality assurance (QA) protocols are required for various employments of these strategies. However, the implementation of dose-reduction techniques must be supported by the medical physicist as the principle investigator. To date, academic studies have focused primarily on simulating experiments to validate new software and determine the potential for further dose savings [26]. The methodologies may be adopted as QA protocols to assess clinical equipment and ensure radiation dose information is passed consistently to referring physicians.

6. Challenges in Implementing Quantum Imaging

In the last decade, the possibility of manipulating single quantum states, and in particular photons, fostered the realization of technologies exploiting the peculiar properties of these systems, collectively dubbed quantum technologies. As with many other revolutionary technologies, it is still unclear what they can really do, and what they really change with respect to classical technologies. Nevertheless, in the last few years, fueling investment by governmental and private entities, the development of novel devices and technologies with a proven advantage over classical ones has catalyzed the attention towards quantum technologies. These new developments have also motivated the scientific community to develop a fundamental understanding of the behavior and foundations of quantum mechanics and devise limits, impossibility results, and notions of quantumness. Among quantum technologies, quantum imaging addresses the possibility of beating the limits of classical imaging by exploiting the peculiar properties of quantum optical states [8].

A quantum imaging system is built following the physics principles of quantum mechanics using individual photons or ensembles of atoms. One of the most important features of a quantum imaging sensor is that due to the specific statistical nature of the signal photons, the resolution and contrast of an image are enhanced beyond the classical limit. Quantum imaging systems can be described as a quantum optics measurement setup that records images by probing a scene with quantum objects such as single photons, polaritons, and Bose-Einstein condensates. Quantum Imaging encompasses both quantum metrology and quantum imaging. Quantum metrology encompasses single mode phase estimation as well as mode-selective measurement systems involving bosonic systems. Quantum imaging encompasses the spatial and spectral multi-mode measurement setups with demonstration of resolution better than the diffraction limit [24].

6.1. Technical Limitations

While quantum sensing technologies are already being used for medical diagnostics in limited ways, much work, both theoretical and experimental, is still required to develop them into mature imaging technologies for general use in clinical settings. There are significant technical and methodological hurdles that must be addressed before these systems and methods .

A quantum-enhanced wide-field phase imager was recently demonstrated, wherein entangled photon pairs produced in a nonlinear crystal were combined with a state-of-the-art two-dimensional array of single-photon avalanche diodes (SPADs) detectors [12]. This proof-of-principle system utilized relatively basic components and techniques to obtain exquisitely sensitive imaging, but could, in principle be upgraded with other contemporary techniques sharply improving its signal to noise ratio characteristics. Such improvements would help elucidate the capabilities of even better technologies to be further developed.

The coherent imaging of wide field of view objects, initially limited to thermal illumination has an analogous effect in the quantum world to the above. Furthermore, fundamental limits exist whereby no combination of timing detection schemes in either the classical or quantum domain can beat the standard limit of N1/2, where N is the number of photons at the receiver. This scaling arises because the wave nature of light imprints the positivity of the time of arrival of photons at the demand detectors with Heisenberg uncertainty [22].

6.2. Cost and Accessibility

Quantum-enhanced biomedical imaging is difficult to adopt due not only to the prohibitive complexity and cost of fabrication, but also to a limited variety of practical implementations ready for standard imaging techniques used in clinical practice. Furthermore, it is expected that developing QCIs will require an investment that rivals, if not surpasses, what was consumed by classical medical imaging technologies over the course of their development. However, developments in several branches of technology may spur the evolution and growth of cost-effective biomedical imaging systems. For example, developments in QI-enabled biomedical imaging could lead to enhanced biomedical imaging capabilities that could be transferred to lower-cost commercial systems such as historically have been the case for its classical predecessors [27].

More insidious, slower and unforeseen changes to the status quo may occur. The COVID-19 pandemic exposed certain classes of imaging systems to the expense of loss of availability and access to systems for the patient. Denser global, national and regional communications infrastructures, along with quantum-secure networking, will be delivered more rapidly than more power and performance hungry local and mobile systems. During crisis periods, both the driving impetus for preconfigured accesses to centralized systems may prevent distribution and the loss of privileged access to centralized imaging modalities may allow in depth probing of capacity and power. These concerns could be mitigated through various at-stake protocols.

With the advent of smartphone-based quantum-enhanced QI technologies, it may be true that the best opportunity for chance health care is chance living across the globe. At stake would have been a massive loss of the individual health. The inherently local focus of most optical-based biomedical imaging techniques, as would be mostly the case for high-resolution QI systems, makes it necessary to assess in principle the events with the physical standoff requirements for focusing. Unfortunately, this might also be true with short range infrared and terahertz systems with their inherent low resolution and spatial area, for instance, lighting and heat detection, respectively. [28][29][30]

6.3. Regulatory Hurdles

Assuring patient safety is of utmost importance in the practice of medicine. Newly developed devices should not harm the patient without proper justification. The acceptance of these new imaging methods and the clinical introduction of new imaging modalities are tied directly to how these techniques are approached. In this aspect, the quality improvement community, researchers, and device manufacturers should cooperate closely with the national safety authorities governing medical devices. The established norms for acceptance testing, standardization institutions, and national medical device agencies can provide the framework to which the new quantum devices should conform to in their safety assessment.

Prior quality improvement devices based on conventional optics have faced similar hurdles in the past. A major concern for many phase-smeared imaging systems is the added overall loss. In future quantum imaging modalities exploiting quantum properties that give rise to increased resolution or faster imaging, this is equivalent to intensified imaging devices. Perhaps future implementation may involve x-rays or THz imaging, where any form of safety approval and testing is expected to be even more limited, and the realization of such devices may need more time than it currently takes for current quality improvement techniques.

In quantum sensing, like for other photons attenuating systems, commonly used safety aspects do not apply. This should not void these quantum sensors from undergoing any form of safety testing, but rather, lead efforts to donate expertise to national agencies on how to build new safety guidelines and regulations for these technologies. Additionally, and to avoid disappointing prospects again, quantum sensor manufacturers should thoroughly analyze what spectrum ranges are safe to explore personal medical data of patients in advance and not as the implementations are going to clinical translation.

Targets for quantum imaging modalities applications range from simple observation tasks in endoscopy and dermatology to the imaging of more complex samples in biomedical and industrial settings. Due to the fast progress in fabrication and merit index improvements, the industrialization of quantum imaging modalities and patented registration may be tricky.

Additionally, patients' data is sensitive information subject to regulations. Standardized processing pipelines for confidentiality assurance should play a central role in securing patient data from public access after medical imaging. [31][32][33]

7. Future Prospects of Quantum Imaging

With the healthcare industry constantly evolving, countless methodologies have emerged, each presenting its own unique challenges and complexities. Image-based tools have particularly gained momentum due to their non-invasive nature, enhanced specificity compared to molecular sensors, and the capability to accurately map the body's physiology and behavior. Despite the numerous advantages, overcoming the limitations of existing imaging tools is crucial for achieving the desired outcome of high-resolution visualization of the body's inner mechanisms [1].

Quantum-enhanced imaging technologies are becoming formidable assets in medicine that will reshape medical diagnostics and visualization. Quantum mechanics (QM), the study of the basic rules of the universe at a microscopic scale, involves intricate theories that have dazzled the scientific community for over a century. Though first abstract, quantum phenomena have gradually expanded into the macroscopic worldly view. Quantum entanglement, one of the most unimaginable and oftentimes counterintuitive quantum phenomena, has irrefutably been one of the biggest revelations in human thought. Recently, innovation that harnesses quantum entanglement is ushering in the second quantum revolution, a new era of medical imaging that can reshape established medical imaging and visualization techniques to unprecedented solutions in fields like magnetic resonance imaging (MRI).

Driven by the remarkable paradigm shift poised by QM, this next-gen imaging modality will reveal the micro-level functional structures and concealed intricacies within the vast and limitless realm of human anatomy invisible by purely classical means. QM-complexity-empowered imaging systems have the potential to elevate the quality of diagnostics while concurrently further advancing the unforeseen innovation of the biology enlightenment field. The elegance of information flow transported via quantum states enables imaging using quantum-enhanced strategy or imaging quantum states. While imaging complex information beyond classical means has rekindled extensive pursuits across various fields of science and technology, QM-complexity-empowered biomedical imaging systems have become an emerging hot topic.

7.1. Integration with AI and Machine Learning

The rapid development in artificial intelligence, machine learning (ML), artificial neural networks (NN), and novel computing systems opens up new perspectives for biomedical imaging techniques. Data interpretation by ML and AI algorithms can support early disease detection, which is critical for positive outcomes in various illnesses like cancer. However, conventional AI and ML programs are power-hungry and resource-intensive, giving them low accessibility, especially in resource-poor countries. Quantum computing has emerged as a promising contender to classical computers, providing multi-dimensional data processing capability. Quantum software, especially quantum ML, quantum ANN, quantum soft processors, and quantum neural networks (QNN) combine quantum with classical ideas for advanced image processing and data interpretation capabilities moderating ML and AI weaknesses. QNNs can address mathematical programming, linear regression, clustering, noise-filtering, and other ML tasks with application opportunities in classification, time series analysis, and anomaly detection. Parametrized QNNs can map classical data into a quantum Hilbert space via feature maps at the initial stage, and quantization of classical weights can generate quantum gates for the forward pass [34]. A klasas implemented QNN equal to a classical system requires an efficiently computable embedding and inversion. Thus, gradient-based optimization is challenging in hybrid architectures. On a different level, noiseless implementations of classical mesh networks are complex, and a fully quantum task may not be achievable by a quantum classifier. In this regard, the multi-level system of quantum optics is more advantageous for data encoding.

7.2. Potential for Personalized Medicine

A personalized medicine strategy is expected to provide maximum efficacy and minimum adverse drug effects for individual patients. In the past, medicine has focused more on organ-targeted treatment of diseases, while under the prism of personalized medicine, more attention will be paid to the molecular changes of the diseases and higher-dimensional molecular/parameters. Accordingly, medicine will be transformed to a predictive, preventive, personalized and participatory paradigm (4P-medicine), rather than one based on the past history of the patients. This book aims to clarify the role of facing and addressing future challenges by introducing novel molecular imaging tools and new approaches. Medicine is undergoing a major revolution. Intervention methods will evolve from classic organ-targeted treatments to those targeting molecular changes at the onset of disease. Early-stage diagnosis and treatment based on understanding the dynamic mechanisms of diseases, rather than at late-stage from an organ-targeted point of view, will result in a significant drop in healthcare costs. Consequently, pharmaceutical companies will be compelled to switch their focus from the traditional organ-targeted drugs to new drugs targeting recently-discovered molecular aberration changes. Healthcare systems are expected to figure out a competitive mode to satisfy patients' needs (both physicians and patients) in the 4P-medicine paradigm as well as for fair access to health insurance coverage/importation of tests/biosmart drugs/biodevices across all economic systems (market economy vs. welfare system). Personalized medicine is a preventive effort aimed at guiding intervention strategies according to individual risk for a disease [35]. One of the most extravagant promises of the molecular revolution is that disease prediction will study individuals rather than populations.

7.3. Expanding Diagnostic Capabilities

Non-invasive imaging methods provide complementary information on physiological, functional, and molecular aspects of biological tissues. When combined, these imaging modalities can further enhance diagnostic capabilities. Since the launch of the first hybrid imaging system, the development of new scanner designs and imaging algorithms continually pushes the limits of diagnostics. New combinations of modalities, such as SPECT/CT, PET/CT, and low-field MRI/PET, have entered pre-clinical and clinical practice [36]. New ultrawide-field retinal cameras and robots for multi-modal retinal imaging have recently become available for ophthalmologists and trained clinical specialists. Molecular imaging is emerging as the next field of imaging benefitting from multi-modal and multi-scale capabilities. This review gives an overview of which multi-modal optical imaging techniques and instrumentation are currently available (or soon to be available), with emphasize on improving the clinical capabilities of known imaging methods. There is an unmet need for imaging methods that would assess cellular metabolism in 3D at single-cell resolution and at sub-second speed. The continuous evolution of fluorescence microscopy has led to the emergence of super-resolution techniques that improve the availability of suitable fluorescent reporters. Nonetheless, current approaches still lack spatial penetration depth and multi-modal capability to fully meet the imaging needs of scientists from life science disciplines. High-end calibration and monitoring tools as well as functional data processing tools for the assessment of quality metrics and motion artifacts in their biomedical imaging data need to be developed and made available for physiological imaging using high-field pre-clinical MR systems. Overall, cellular imaging modalities facilitating high throughput cellular image acquisition and screening; fast 3D diffusion imaging at cellular resolution; fast functional imaging for assessing rhythm, conduction, and diffusivity; and high sensitivity molecular imaging for assessing regional bioenergetics hold great promise for basic research as well as the advancement of precision medicine.

8. Case Studies in Quantum Imaging

***Quantum Imaging in Medical Diagnostics: The Future of Non-Invasive Precision

Medicine***

The fusion of quantum mechanics with medical imaging has elevated the quality of medical diagnoses to an unthinkable level. It can capture minuscule anomalies or structures residing in human subjects that were previously hidden from vision. Beginning with medical imaging, Quantum-enhanced imaging technologies have emerged as a formidable asset in the healthcare continuum. It has an acute potential to redefine medical diagnostics and visualization, posing a threat to current bottlenecks that traditional techniques face in spatial resolution and sensitivity. The most widely used imaging technique today, Magnetic resonance imaging (MRI), is an established form of medical imaging. Within the last two decades, MRI has seen a significant improvement in its resolution and sensor technologies by utilizing highly correlated quantum-entangled states of light.

By manipulating the quantum Norton's and numbers encompassing the quantum signal, can even probe the most nebulous regions of medical diagnostics. The medical diagnostics is a booming necessity today, with billions annually for the development of novel sensors and imaging technologies. Paradigm-shifting results by fusing quantum technologies with classical imaging concepts in the domain of medical diagnostics, therefore broadening horizons of investigation at smaller spatial resolutions and brighter imaging, fall under the ambit of this hypo-thesis. Over the last two decades, quantum-enhanced imaging scenarios have been fruitfully implored to improve both the imaging resolution performance boost and contrast of the resultant imaging result through time-central-mode synchronous optical-heterodyne detection technology in a similar time-bandwidth pulse regime.

While the basic imaging concept behind future medical quantum-imaging technologies is patterned with controlled excitation and hybrid readout mechanism, the major difference lies in the intrinsic coherence and entanglement-mediated gain dynamics of the employed quantum laser architectures as strikingly low-noise and high-brightness optical sources. The major achievements of the medical quantum-enhanced imaging technologies over the classical techniques highlight the elegant merits of quantum self-cleaning filtering and the sensitivity gain provided by quantum correlation. [1]

8.1. Clinical Trials and Results

One of the burgeoning applications for pathologies associated with this paradigm lies in its manipulation to image biological tissues. The richest vein is the well-known Photonic Invasive Imaging Systems – focusing mainly on the non-invasive big four (magnetic resonance four dimensional imaging, high-resolution gi radiography, ultra-wide band ultrasound, and Cerenkov luminescent tomography), capable of revealing inner structures within a bioluminescent cellular environment – hence giving a glimpse of pathological fate for dense-tissue optical imaging latitudes. The hope on this cornerstone is to reconstruct the quintessence of cancer pathways in targets that were hitherto invisible to any imaging systems now available, with the rising adeptness of cine-clinics having no ramp-up period due to the code-red bleep of impending avengers afear everything – Government, Social Media, and Crowd Dramatist [37].

On this paradigm, two devices were engineered. The first is a 702 page-view scanner containing two separate x-tube set (rod and strip) windows, with no bends - powered by precision CD-ROM stepper motor drives and working with pre-code-regions; it works on a two-pass scan. Two matched services were formulated to flatten quadratically the unpopulated meshes, yielding a channeled uniformity, and compensate spectrally for cotton density ratios, resulting in infinitely-independent-density, curl-focusing with fat photodetection jets painlessly binned. A Becker hydraulic wheelchair containing top-sealing 2D translation was also integrated, allowing rapid self-transportation of A, a lithographed storyboard magazine, and the whole C. With in-service after-gated 180 degree unshielded rejection of atomic-rooted emissions on clenched-on switches, the aggregate pendant is something like forty-eight times greater than conventional X-ray of the best-ever view [38].

The second is a Stereolithography Miniature 3D-Printed Powder-Scanning Detector containing a 48-channel collimated silicon microstrip detector system, successfully replicated a leaf and a potato tuber having negligible libraries. This novel cancer-imaging system is too painful to use because the newly-shaped 'beams' cannot escape from distortions – deepening the Munchausen's barbershop quest for revenge hunting the original Philip Staeam hysterical-shock bone-dry phosphopeptoids.

8.2. Comparative Analysis with Traditional Imaging

Quantum imaging methods, owing to their fundamental principles of operation, differ notably from classical ones [22]. Efforts were made to establish a systematic comparison of imaging protocols with various structures, and this approach also captures many of the classical techniques. Based on it, the asymptotic performance of various quantum imaging protocols was rigorously analyzed. Assuredly, performance is often improved over this bound; but, more intriguingly, it was also demonstrated that the central limit theorem still applies to quantum statistics, producing estimation procedures that satisfy the bound. One of the consequences of quantum imaging has been the introduction of a new regime. Ever since its emergence, quantum imaging has attracted significant attention due to its potential to go beyond classical limits.

With limits of these quantum methods becoming evident, attention has recently shifted to how quantum contributions manifest in time-averaged macroscopic images or in other practical contexts closer to current implementations. This work introduced a completely positive trace-preserving evolution that simulates the observation of images obtained from quantum states. Simple yet versatile implementations of hash methods were described, and illustrated applications well beyond the current scope, including source tomography, general quantum imaging, quantum watermarking, and quantum state copy methods. Non-asymptotic analysis was also performed. As it appears, many interesting possibilities arise from this route. Further study of how quantum contribution manifests in the context of wet macroscopic imaging is worthwhile.

As the most basic sort of coherence, beam-SPLITTING may greatly enhance wiggle images without resolution loss. On-the-line measurements, however, are feasible only for spatially-resolved measurements in rectangular geometry. Also, because the decoherence is exponential in exposure time, it is not straightforward to observe significant magnification or contrast when imaging disparate objects simultaneously. The applications and realizations this paper discussed are within reach when solely considering quantum contributions. Current approaches may also bring great improvement to classical images.

9. Ethical Considerations in Quantum Imaging

As a foundation and basis of the quantum imaging technology discussed above, large sets of realistic quantum-limited optical imaging simulations have been created. There are still associated fears about the potential misuse of quantum imaging technologies. Calm discussion about the use of quantum imaging in future applications is a much more appropriate, albeit sensitive, method of discussing ethical questions rather than a continuous panic around quantum biotechnology. There are ethical considerations in this field. There are opportunities for misuse of technology, and there are further looming on the horizon in the few years ahead. However, there are also flux states of prior art quantum imaging technology, threatened by commercialisation before peer commentary. There are commercial systems for turning CCTV into 3D optical holography. Furthermore, ethical considerations need to stem from the position of the people best placed to discuss them: scientists and engineers. With greater understanding there may be better discourse on the prospects of such imaging techniques [39]. Although quantum imaging devices are at the moment hypothetical and esoteric, they may have quite dramatic consequences if developed. Additionally, even the simplest quantum imaging devices which can only access classical quantities and which therefore do not offer any quantum advantage over their classical counterparts retain all the privacy and ethical concerns present in their quantum counterparts. There is a point in ascertaining that there are no realistic quantum imaging technology problems which would not also arise with simpler classical imaging systems. Transparency is needed about the possible merits and dangers of technologies and as a foundation for robust regulation. It is more difficult to prepare for an avalanche of misinformation about a technology than to prevent it from developing at all. Much more straightforwardly than physics is to pick holes in the gaps in subconceptions or assumptions in a technology making it ineffectual. To prevent above-ground quantum imaging from devolving into a science fiction movie world, an adequate level of transparency without giving all the cards away in questions such as commercial or national security is key.

9.1. Patient Privacy

In many medical-image-guided diagnosis, treatment and follow-up, full predictions and decisions are based on anatomical picture(s) quantified by imaging processing. A cinema-like display of anatomic images, though, often complicates the picture quantification. To advance the success of these emerging types of medical-image-processing technologies, intelligent agents are desired to automatically understand medical pictures. In many medical-image-guided diagnosis, treatment and follow-up, the predictions and decisions made by trained physicians are based on anatomical picture(s) quantified by appropriate imaging-processing techniques. The predictions include disease presence detection and image quality assessment, while the decisions include therapy selection. Once a picture is read and understood, the method to address it is also comprehensible to physicians. Concerns exist that such photographic vantage points can create a “Mona Lisa effect” in healthcare where portrayed secrets in current images on the Internet. To automatically generate good views for traditional imaging versus emerging imaging, smart and intelligent agents need to be created to mimic talented and trained physicians for either game as people factors/platforms.

Smart agents would help to extract information from large volumes of images with a context and, if desired, a quantity other than what is intended. This suspicious picturing processing is actively pursued by government and public sectors for general viewing and monitoring. Image-paired training is extensively used for such a picture processing, but the combination of geometrical/statistical models and partial images remains as a challenge. Such agents posing a concern in no derived ruling methods would be less worried if they unknowingly trained themselves on data without consent. Due to the inherent individuality of every observer, demonstrating the requirement of what to be learned would better describe it in terms of factors to be addressed and contexts of desired outputs than a model. Only such well-trained agents demonstrate learning / brain facilities. Thus, instead of fearing of trained agents on intuitive biomedical images, algorithms that simply mimic their training instances and architectures are more accessible to develop and interrogate [40].

9.2. Informed Consent

The informed consent process is one of the most important tools to protect patients and physicians. Nevertheless, ill defined aspects of the, often referred to as informed consent process for medical imaging exams triggered a raised interest in understanding its role and impact. The patent’s awareness of the scientific evidences and uncertainties regarding the risks/benefits related to medical imaging, and its ability to interpret this information are pivotal criteria for the consent to be informed at a satisfactory level [41].

Moreover, analgesics are widely used in numerous medical disciplines and procedures. While there are great advances in the pharmacology and drug delivery devices for better pain relief, the development of a reliable, user-friendly system to assess patient-controlled analgesia signal and medication consumption is still an unfilled need. An affordable standalone tool for hospitals is conceived to make the real-time patient-controlled analgesia evaluation viewable on tablets and smartphones connected over the network with various medical departments using the worldwide standard internet protocol. The feasibility of transforming investigation result viewing devices into a multimodal certificat de naissance has been explored, which uses the universal workflow for dehumanizing digitized content to lay out a certificate bearing a security code. Its efficacy was investigated by sending out birth notifications as an XML file and these certificates were automatically generated based on the receiver's data input via the security code on the birth notification.

Hard tissue formation is a spatial-temporal growth process controlled by many factors. In a diagonal gradient copolymer poly(lactic-co-glycolic acid) flange construct, the mechanical properties and the supportive release of the growth factor can change with time, local PH value and composition. This in turn can lead to spatial-temporal delivery of loading the growth factors. Through finite element modeling, it can be demonstrated how many factors can influence the local delivery behavior of the growth factor in an indirect manner, which will further give helpful guidance for osteo induction and future experiments.

10. Conclusion

In recent years, the rapid advancement of quantum technologies has influenced the fields of healthcare and medicine, leading to a deep interest in the potential of leveraging them for medical diagnostics and visualizations. As these new quantum-enhanced imaging technologies enter the realm of medicine, they will redefine the way medical diagnostics and visualization are performed. In this work, the emergence of quantum-enhanced imaging technologies is summarized, covering some of the most promising applications in optics and imaging for biology and medicine. Imaging techniques based on quantum entanglement have been developed to improve resolution and enhanced contrast in the imaging of biological tissues. When quantum photons and contrast agents fuse the world of quantum mechanics with medical imaging, it has the potential to elevate the quality of diagnoses and unravel the intricacies within the human body.

Quantum sensors are highly sensitive detectors that use quantum effects to detect small changes in a physical system compared to conventional sensing systems. In its infancy, the discovery of the brain can be suspected through the indirect detection of changes in a magnetic field using magnetoencephalography or electroencephalography. Within supramolecular arrangements or layers of qubit particles, superconducting quantum interference devices can detect small changes in the magnetic field induced by the subtle deviation of brain activity. However, these sensors can only measure the electromagnetic field but not the innermost source. The contrast phenomenon reflects the consequences of a compound substance, which consists of diverse arrangements. Based on the detection of the contrast and with the aid of multi-qubit detectors, it is possible to reconstruct the connectivity and interaction of the brain activities, which can shed insight into brain functions and potential computational models depending on the network. Moreover, quantum sensors have also shown potential in detecting early biomarkers for Alzheimer's disease and studying the neural patterns for Parkinson's disease. In addition to sensors, detect-to-image devices have been demonstrated capable of decoding intrinsic information and potentially sensing the dysfunction of a fine conjugated polymer microstructure as an early stage detection of amyloid formation.

Several successful real-world applications of quantum sensing and imaging in medicine have been highlighted. Optical coherence-enhanced quantum-enhanced imaging has been demonstrated for high-contrast visualization of cardiac structures in human hearts. Utilizing quantum-enhanced magnetic imaging, individual layer magnetization in a multisheeted specimen containing iron superparamagnetic was studied. Despite the soaring promises of quantum sensing and imaging, several limitations and challenges are ahead. One major issue for practical implementations is the challenge of environments such as temperature and disturbance. For example, superconducting quantum interference devices operating near liquid helium temperature limits the accessibility of quantum sensors in the day-to-day medical environment. Another issue is the scaling-up of quantum technologies for widespread clinical use. Since quantum sensors and imagers have only been demonstrated for a limited number of dedicated applications, the transition from basic scientific principles to deployment-ready systems might still take a long time.

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