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Recent Progress in Nanometrology Techniques for Object Characterization

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ABSTRACT

The importance of true micro and nano characterization is required for advanced metrological techniques. The ability to measure and characterize the dimension, geometrical form and surface topography to study physical, chemical, mechanical and biological properties for complex features of engineering object, biomaterial, organ, tissue in micro- or nano-meter scale is vital for high degree of precision and accuracy and to verify the quality and reliability. This paper discusses recent progress of the advanced soft coordinate nanometrology techniques. These techniques have the high ability to characterize the dimensions and surface characteristics of proposed objects needed to identify their various types and applications. Moreover, it is important to note that the ultimate aim of these advanced techniques is to understand and predict the object behavior of synthesis and natural particles. The surface characteristics of biomaterials are also obtained and summarized in details.

Keywords: Dimensional and surface metrology, object characterization, TEM, SEM, STM, AFM, CMM, CT and Raman techniques.

I. INTRODUCTION

Advancement in micro- and nano-technology revolution is the only way to understand resolving and development of the engineering problems. Nanotechnology cannot be developed independently without progress of metrology in nanometer scale. The science of measurements and its applications at the nanometer scale is called nanometrology. Although novel and surprising properties of nanoparticles are the basics of material nanostructure, they excite scientists to put them often in the hand for general public applications. Advanced materials raise the issues of dimension and surface metrology techniques to give unexpected analysis and new production [1-2]. Some problems in the biomedical applications are medical devices, health safety, electronic sensors and monitoring systems. More specific problems such as biocompatibility, functionability, antitoxicity, sterilizability, patient satisfaction and manufacturability are important issues to satisfy the design requirements of nanobiomaterials [2-3]. In nanomedicine applications soft nanometrology techniques are playing important real role for characterization of viruses, living cells, nanoparticles, strands of DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). Also, they include organization for cell sorting, cell manipulations, tracking of bacteria movement and red cells. Similarly, repairing bones, implant of soft and hard tissues, artificial tooth development and cavity repair are important applications, where the greater control in nanoscale is required [4-5].

The major objective of this work is to identify the advanced soft coordinate naometrology techniques (ASCNMTs) that can be obtained in nanoscale for object characterizations. These nanometrology techniques are newly using for characterization of engineering objects, synthesis biomaterials and hard with soft tissues. Moreover, in the same time the need for accurate dimension and quality surfaces of objects have become necessary requirement to meet the challenges of modern technology [6]. The ASCNMTs include transmission electron microscopy (TEM), scanning electron microscope (SEM), scanning tunneling microscopy (STM), atomic force microscopy (AFM), laser confocal microscopy, Scatterfield microscopy (SM), coordinate measuring machine (CMM), computed tomography (CT) device and Raman Technique. They are presented and discussed throughout this work to provide advanced applications under the modern heading of dimension, geometrical features and surface topography around the world.

II. ADVANCED SOFT NANOMETROLOGY TECHNIQUES

Metrology is the measurement science and its applications in all life fields, especially in the field of engineered objects. Nature's of the ASCNMTs technology involves miniaturization and integration. The need for accurate dimensional measurements and quality of engineered surfaces has become necessary requirement to meet the challenges of modern technologies. Thus, advanced precise and accurate measuring techniques play a significant role to improve the function and quality of engineered products [4-6]. Advanced metrology is concerned with measurement and its application at the highest level of precision and accuracy. Advances in metrology depend on many improvement factors in scientific knowledge, instrumentation quality.

Science of metrology makes high impact on the overall quality of industrial products, where they depend also on the level of demands from industry. The metrological challenges in nano-science and technology lie in its peculiarity. The laws of physics at this dimension operate in unfamiliar ways to define behavior and imposing constraints on what is possible for design, measure and utilize [7].

Nanometrology is a science and art of measurement involves the manipulation in nanometer scale to create nanostructures with unique dimension and surface analysis methods [7-8]. Metrology method is needed in order to fully characterize nanoparticles perform accurate characterization of nanoparticles and toxicological tests. It becomes well known that nanotechnology holds a great promise for creating new materials with enhanced properties and attributes. The novel properties of various types of intentionally produced nanomaterials enable applications in commercial, medical, military, engineering and environmental sectors. Integral to the emerging nanotechnology enterprise have been identified by the National Nanotechnology Initiative (NNI) as critical nanotechnology areas. Metrology is a vital to applications for electronics in medicine in order to design new nanomaterials at the nanoscale to meet the needs of emerging nanotechnologies. Currently, available equipment in most cases limits the resolution and capabilities required for every area from laboratory research to commercial-scale manufacturing [8]. Nanocharacterization is the measurement of physical and chemical properties such as dimension/size, force composition, surface area, and shape of nanoscale materials and devices. Moreover it includes imaging of the three-dimensional (3D) relationships of complex components [7].

Our concern is the characterization metrology techniques of engineered-nanoparticels correctly which have extra characteristics due to their small size that influence toxicological effect, an exposure risk of any nanomaterial, and other properties of having high surface energies which is not evident in the bulk material of the same chemical composition [9]. The current scientific and technological advancement started by discovery of the TEM, SEM, STM, AFM, confocal microcopy, CMM and CT techniques. The intervening years have witnessed an unparalleled growth in the ability to characterize structures and complex materials at ever-increasing spatial resolution. CT technique is an advanced imaging technique used for complex hidden geometries in 2D and 3D macrostructures of object. The invention of this technique is initiated as revolution in diagnostic technology by allowing users to look inside an object and obtain a very clear anatomical image without violating the outer surface of his body [10]. It uses special x-ray equipment to obtain projected images from different angles, and then processed by computer to present a cross-section of object. The last two decades have witnessed numerous research efforts that sought to provide the capability of metrology techniques to perform measurements of objects in nanometer scale, see Fig.1.

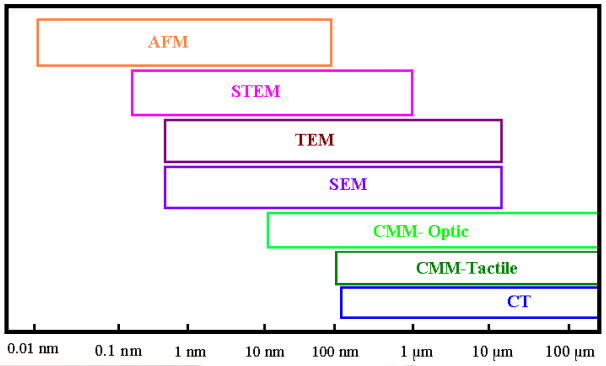


Fig.1: The length scale of advanced metrology techniques

The used metrology techniques for surface characterization in nanometer scale are associated with resolutions, while other different measures and current metrologies show approximate ranges of various measurements are based on the best available information [8]. Bio-nanotechnology (bio-nano) may be considered from two sides: the benefits, and the risks. Risks of bio-nano such as nanotoxicology are very important. The metrology of bio-nano gains increasing importance today since some bio-nano products such as glucose sensors are in near-market or in trial stages. There are three main areas where development of bio-nano is currently taking place, namely: (a) medical devices and implants, (b) nanomedicine and personalized medicine, and (c) biological superstructures and engineered nanobio-materials [11].

Scanning Probe Microscopy (SPM) becomes a broad group of metrological techniques used to image and measure properties of material surface. It involves scanning a sharp tip across the sample surface while monitoring the tip-sample interaction to form a high resolution image [12-13]. SPM standard instruments are now commonly used at scientific and industrial laboratories where Fig.2 shows it's basic components. New techniques are necessary to allow imaging, modifications and manipulations with the developed nano-objects to provide information on differences in friction, adhesion, elasticity, hardness, electric fields, magnetic fields, carrier concentration, temperature distribution, spreading resistance and conductivity [13]. There are a few tens of various constructions based on the general SPM idea. Electrochemical STM (EC STM), magnetic force microscope (MFM), friction force microscopy (FFM) and scanning near-field optical microscopes (SNOM) are the most common among various types of STM

and AFMs. They permit imaging of the surface topography and correlation with different physical properties within a very broad range of magnific-ations from millimeter to nanometer-scale range. The possibility to perform SPM measurements at wide range of temperatures from a few tens of mK to 1400 K has appeared during the last two decades. These new SPM constructions have opened new possibility to follow the phase transitions versus temperature in situ investigations [14].

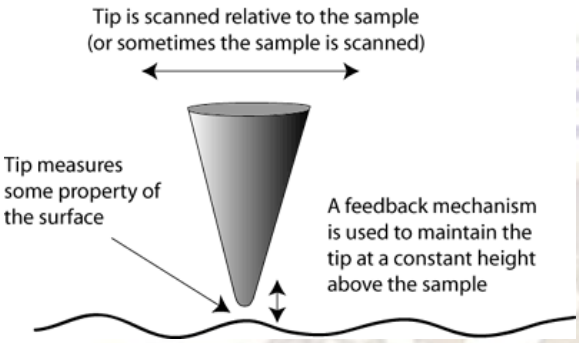


Fig.2: Basic principles of scanned probe techniques [15]

2.1. TEM Technique

Transmission electron microscopy (TEM) is the first type of the electron microscopy instrument used to investigate the internal structure of micro- and nano-structures. It is sophisticated powerful dimensional tool used to form the highly magnified final image. So a fraction of TEM electrons that have to passes through the object sample. Figure 3 illustrates a schematic outline of a TEM technique. The TEM contains four basic parts: electron source, electromagnetic lens system, sample holder, and imaging system. Most of the scattered (or directed) electrons are prevented from reaching the image plane by positioning a small objective aperture located in the back focal plane of the objective lens. This aperture thus serves to determine the image contrast [12]. It can be used as a high resolution scanning transmission electron microscope (STEM), where a finely focused electron beam is scanned across the sample and an image is formed using one of several available electron or spectroscopic signals [16]. TEM theory depends on a transmitted beam of electrons through an ultra-thin specimen interacting with the specimen as it passes through. The image formed from the interaction of the electrons with the sample then is magnified and focused onto an imaging device such as a photographic film, a fluorescent screen, or detected by a CCD camera. CCD camera is a charge-coupled device for the movement of electrical charge. In order to let the electrons pass through the specimen, the specimen has to be ultra-thin, usually thinner than 10 nm. The resolution of TEM is significantly higher than light microscopes. This is because the electron has a much smaller de Broglie wavelength than visible light (wavelength of 400 ~700 nm) [17-18].

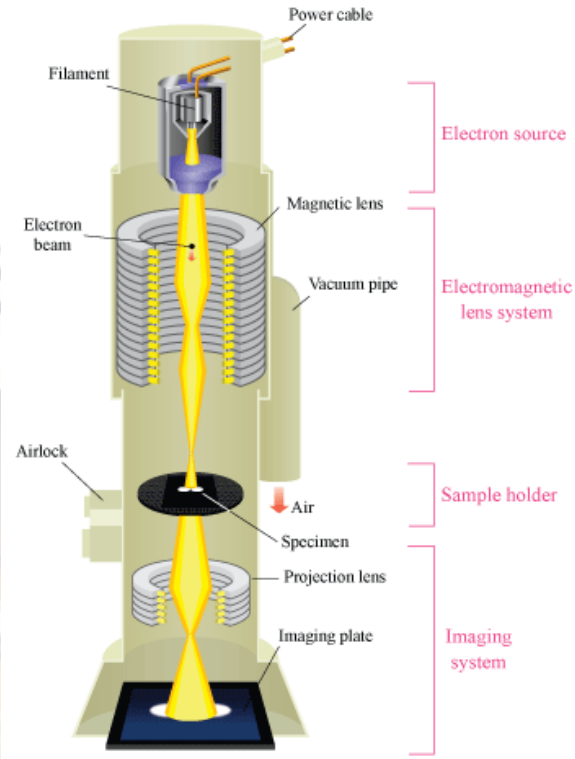


Fig.3: Schematic of TEM basic components [19]

2.1.1. High-Resolution TEM (HRTEM)

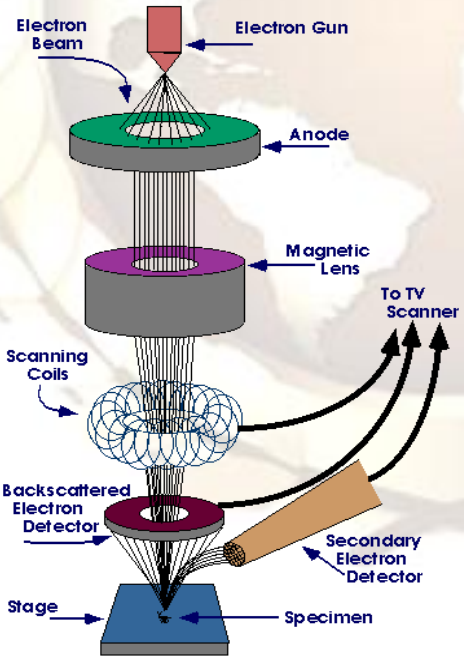
Conventional TEM uses only the transmitted beams or some of the forward scattered beams to create a diffraction contrast image while HREM uses the transmitted and the scattered beams to create an interference image so it is indispensable for nanometrology. HREM has been mainly applied for imaging diffraction and chemical analysis of solid materials such as carbon nanotubes (CNTs) which were first identified by HREM. Conventional imaging and diffraction are the most powerful methods in characterizing the phase structure and phase transformation of inorganic materials based on the assistant of energy dispersive X-ray spectroscopy (EDS) and electron energy-loss spectroscopy (EELS) [18-20]. It contains an array of controls and many adjustable parameters by which only a small number of parameters are needed to be known accurately. Details about the experimental determination of these instrumental parameters can be found in many references and it can be also used as useful method for observing localization of some proteins in a cell on nanometer-scale with direct observation of a receptor for a bioactive substance of small molecular weight by using TEM (transmission electron microscopy). This concept can be widely applicable for the nanometer scale-direct observation of the receptor for any small molecules [21].

Table 1: Advantages and drawbacks of TEM [11]

Advantages	Drawbacks
Accessible size < 1 nm, very high resolution	Expensive and complex equipment
Direct Method	High vacuum is needed
No calibration necessary	Sample preparation
Can be directly combined with analytical methods (e.g. EELS)	Slow: Time-consuming
Any particle shape is accessible	Poor statistics , Artifacts

2.2. Scanning Electron Microscope (SEM) Technique

Many kinds of investigations need ultra-structural examination technique especially in biomedical investigations like cells study especially the interaction between bacterial pathogens and host cells. This technique has to provide a new field of viewing quite large sample in focus [22]. As known, the first SEM was constructed in 1938 by Von Ardenne with restring the electron beam of a Transmission Electron Microscope (TEM) to essentially form a Scanning Transmission Electron Microscope (STEM). In 1942, Zworkin et al. developed the first SEM for bulk samples [23]. The combination of higher magnification, larger depth of focus, greater resolution, and ease of sample observation makes the SEM one of the most heavily used instruments in research areas today. It is a very useful imaging technique utilizing a beam of electrons to acquire high magnification images of specimens with ultra-high vacuum environment having a cold field emitter as beam source [24]. Less than 10 nm beam resolution can be achieved by this. In conventional SEM an electron beam with energy in the range 10-30 kV hits the sample surface exciting a range of signals which are recorded as the beam scans the surface of the sample. The SEM is made of several main components: electron gun, condenser lens, scan coils, detectors, specimen, and lenses as illustrated in Fig.4. Today, portable SEMs are available but the typical size is about 6 feet tall and contains the microscope column and the control console [24-25]. Since 1981, the instrument has been used to calibrate SRM 484 as shown in Fig.5 to calibrate the magnifications of SEMs. A photograph of a SRM484f sample and its micrograph are pictured including left area of the most effective sample of SEM where it will be as thick as the interaction volume; depending on the image technique you are using (typically at least 2 µm).



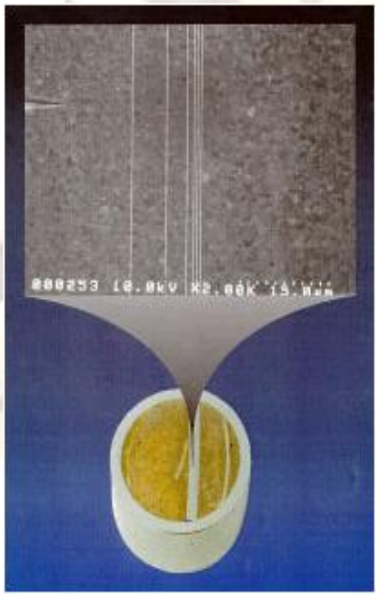
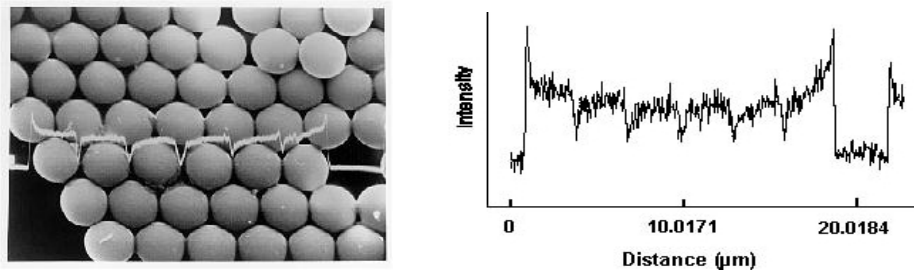


Fig.4: Schematic drawing of basic components of a typical SEM [26] Fig.5: Calibrate SRM 484f Sample [27]

For the best contrast, the sample must be conductive or the sample can be sputter-coated with a metal (such as Au and Ti). Metals and other materials that are naturally conductive do not need to be coated and need very little sample preparation [24-27]. A SEM micrograph of 3µm latex spheres and an intensity-distance plot of a single row of spheres taken with the metrology electron microscope are pictured actually and shown in Fig.6 [27]. Table 2 depicts advantages and drawbacks of SEM.



(a) (b)

Fig.6: Intensity distance plot of a single row of spheres.

Table 2: Advantages and drawbacks of SEM

Advantages	Drawbacks
Inexpensive	Indirect measurement
Fast	Only dispersions can be measured
Good statistics	Influence of medium
No influence of beam	Spherical' particles
Weighting for intensity, volume and number is possible	No model for very elongated or irregular particles

2.3. Scanning Tunneling Microscope (STM) Technique

A Spectacular advances in the development of many artificial materials need to provide new advanced techniques like (STM) which is a powerful instrument used to characterize surfaces and interfaces between engineered structure and allow one to image the sample surface at the atomic level. Fig.7 shows the principle operation of the STM system. STM paves the way for the study of nano-science. Also, it is a microscopical technique that allows the investigation of electrically conducting surfaces down to the atomic scale. The STM provides a picture of the atomic arrangement of a surface by sensing corrugations in the electron density raised from the positions of surface atoms. A fine sharpened tungsten wire forms a "tip", which is first positioned within 2 nm of the specimen by a piezoelectric transducer, and a ceramic positioning device that expands or contracts in response to a change in applied voltage. Although the STM provides sub-angstrom resolution in all three dimensions, it is limited to conductive and semi-conductive samples [23-28].

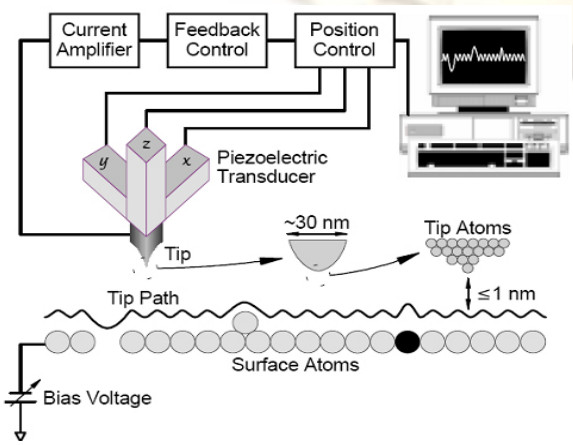


Fig.7: Description of STM operation [29].

For the first time researchers could obtain atom-resolution images of electrically conductive surfaces as well as their local electric structures. Because of this milestone invention, Gerd Binnig and Heinrich Rohrer won the Nobel Prize in Physics in 1986 [28]. The physical key principle behind STM is the tunneling effect in terms of their wave nature, where the electrons in the surface atoms actually are not as tightly bonded to the nucleons as the electrons in the atoms of the bulk. More specifically, the electron density is not zero in the space outside the surface; therefore, it will decrease exponentially as the distance between the electron and the surface increases. So when a metal tip approaches to a conductive surface within a very short distance normally just a few from their perspective electron clouds will start to overlap and generate tunneling current if a small voltage is applied between them [28].

2.4. Atomic Force Microscope (AFM) Technique

AFM was invented by G. Binnig and coworkers at Stanford University in 1986. Since the development of AFM dramatic change have been achieved through opening the door to imaging materials as a device that can provide structural information at sub-nanometer resolution on biological samples of interest so it has high-resolution form of scanning probe microscopy, and also known as scanning force microscopy (SFM). In biomaterials science and engineering applications has increased rapidly over the last few years, AFM has made significant contributions to various biomaterials research areas dealing with the structure, properties, dynamics and manipulation of biomaterials surfaces and interfaces [30-31]. To image insulators as well as conductors, the AFM was developed in 1986. The first commercial AFMs were produced in 1989 by Digital Instruments. In the same time, AFM provides

3D surface topography at nanometer lateral and sub-angstrom vertical resolution on insulators and conductors [23]. AFM creates a highly magnified three dimensional image of a surface. The magnified image is generated by monitoring the motion of an atomically sharp probe due to scan across a surface. It is usually used to study the topographical morphology of these materials. By measuring the thickness of the material, it is possible to determine if bundling occurred and to what degree. Other dimensions of the sample can also be measured such as the length and width of the tubes or bundles. It is also possible to detect impurities. These impurities can be carbon coated metal, amorphous carbon, or other allotropes of carbon such as fullerenes and graphite. These facts can be utilized to compare the purity and homogeneity of the samples made from different processes, as well as monitoring these characteristics with performing different steps or reactions on the material. With AFM, it is possible to measure more than the physical dimensions of a surface because there is a physical interaction of the probe with a surface. By lightly pushing against a surface with the probe, it is possible to measure how hard the surface is where the probe glides across a surface to measure the surface friction [32]. Figure 8 shows the principal operation of AFM. There are different types of AFM with respect to mode, contact mode, tapping mode and noncontact mode. Some other researchers have added a fourth type of mode which is torsional resonance mode [21-32].

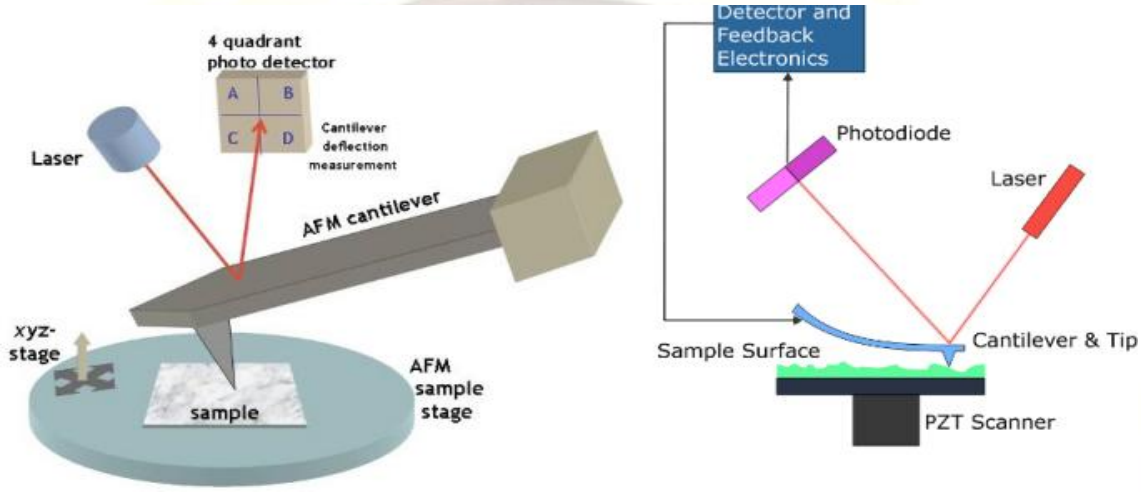


Fig.8: Operation of AFM surface analysis [6, 11, 12, 14]

Table 3: Advantages and drawbacks of AFM [11]

Advantages	Drawbacks
Fast	Statistics problematic
Equipment readily available	Strong influence of the tip possible (size, shape, material)
Inexpensive	Influence of the NP material possible (by tip-particle interaction)
Very high resolution	Particles have to be on a flat substrate surface

2.5. Confocal Microscope Technique

Advanced confocal microscope (ACM) is a relatively new technology, combining high-speed parallel data collection with advanced modeling and measurement routines to acquire and render a comprehensive 3D model of the sample surface, with sub-micron detail, in seconds. Confocal microscopy provides spatial resolution in the Z-direction by using an aperture to exclude from detection light that does not originate in the focal plane of the optical system. Laser scanning confocal microscopy has become an invaluable tool for a wide range of investigations in the biological and medical sciences for imaging thin optical sections in living and fixed specimens ranging in thickness up to 100 micrometers. Figure 9 shows typical components of ACM. The basic optical microscope utilized by Schleiden and Schwann in 1838 is still in use today. Many improvements in the optical design and manufacturing process have refined the light microscope for maximum practical resolution. It becomes known that confocal microscopy achieves dramatic increases in resolution by physical means [33-35]. Confocal microscopy was invented by Marvin Minsky in 1957 and subsequently patented in 1961. Minsky was trying to study neural networks to understand how brains learn, and needed a way to image these connections in their natural state (in three dimensions). He invented the confocal microscope in 1955, but its utility was not fully realized until technology could catch up. In 1973 Egger published the first recognizable cells and the first commercial microscopes were produced in 1987 [36].

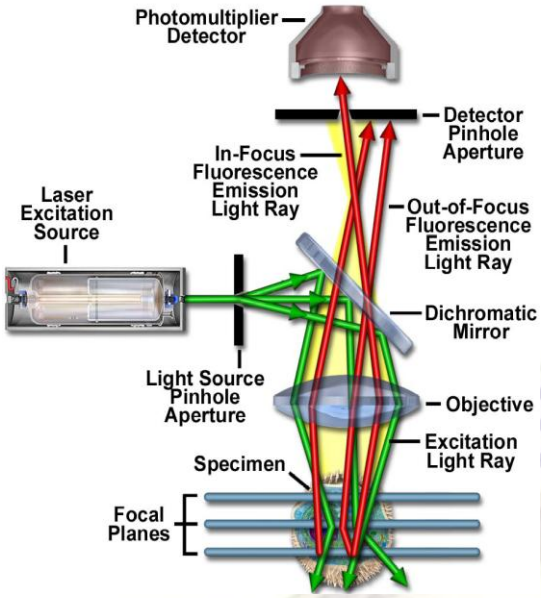


Fig.9: Schematic diagram of the optical pathway and principal components in a laser scanning confocal microscopy [33].

A confocal microscopy generally consists of a laser, pinhole aperture, dichromatic mirror, scanning mirrors, microscopy objectives, a photomultiplier tube, and computing software used to reconstruct the image. Recent advances in laser technology have made lasers in the UV-visible and infrared more stable and affordable. A laser allows for a monochromatic (narrow wavelength range) light source that can be used to selectively excite fluorophores to emit photons of different wavelengths. Sometimes filters are used to further screen for single wavelengths The principle operation of confocal microscopy is done by passing the light through a dichromatic (or "dichroic") mirror (see Fig.9) which allows light with a higher wavelength (from the laser) to pass and reflects light of a lower wavelength (from the sample) to the detector. This allows the light to travel the same path through the majority of the instrument, and eliminates signal due to reflection of the incident light. The light is then reflects across a pair of mirrors or crystals, each one for the *x* and *y* directions, which enable the beam to scan across the sample. The speed of the scan is usually the limiting factor in the speed of image acquisition. Most confocal microscopes can create an image in 0.1 - 1 second. Fig.10 usually shows the sample in raster scanned quickly in the *x*-direction and slowly in the *y*-direction. For microparticle characterization confocal microscopy is very useful for determining the relative positions of particles in three dimensions [36]. Table 4 presents the advantages and drawbacks of confocal microscope technique.

Table 4: Advantages and drawbacks of confocal microscopy [37]

Advantages	Drawbacks
Less haze, better contrast than ordinary microscopes.	Images are scanned slowly (one complete image every 0.1-1 second).
3-D capability.	Must raster scan sample, no complete image exists at any given time.
Illuminates a small volume	There is an inherent resolution limit because of diffraction (based on numerical aperture, ~200 nm).
Excludes most of the light from the sample not in the focal plane.	Sample should be relatively transparent for good signal.
Depth of field may be adjusted with pinhole size	High fluorescence concentrations can quench the fluorescent signal.
Has both reflected light and fluorescence modes	Fluorophores irreversibly photobleach.
Has both reflected light and fluorescence modes.	Lasers are expensive.
Can image living cells and tissues.	Angle of incident light changes slightly, introducing slight distortion
Fluorescence microscopy can identify several different structures simultaneously	---
Accommodates samples with thickness up to 100 μm.	---
Can use with two-photon microscopy	---
Allows for optical sectioning (no artifacts from physical sectioning) 0.5 - 1.5 μm	---

2.6. Raman Spectroscopy Technique

Raman spectroscopy is an invaluable technique for biomedicine investigations and attractive goal in biomedical research. It is a development of a safe non-invasive method for monitoring deep inside living tissue, diseases diagnosis, drug delivery, artificial implantation and cancer detection. Until recently, conventional Raman spectroscopy has the ability to provide extra chemical information below the tissue surface. Thus, many tissue components, such as vines, bones and subsurface cancerous tissue were inaccessible

without invasive methods. Raman spectroscopy is based on an inelastic light scattering by molecules. Raman scattering process depends on photon interaction with a molecule and then scattered into surroundings in all direction. During the brief interaction with molecule, photon loses or gains energy which is then detected and analyzed [38-39].

2.6.1. Raman scattering microscopy technique

A new advanced metrology technique witnessed combining between Raman microscopy and scattering microscopy (scatterometry, SM), forming Raman scattering microscopy. This provides higher spatial resolution due to shorter excitation wave lengths. Significant dimensional information with sensitivity to features up to one-twentieth the measurement wavelength can be extracted from the analysis of scattered light profiles through the use of structured illumination specifically engineered targets and physics-based image process modeling as shown in Fig.10. This concept will be applied to making measurements of line width, line spacing, line height, super-resolution overlay metrology, and defect metrology. Application of SM will extend the resolution limits of current technology by at least a factor of ten [36]. Key project is running to include completion of the 193 nm scatter field optical technique platform and demonstration of full instrument operation in a clean room environment with controlled temperature.

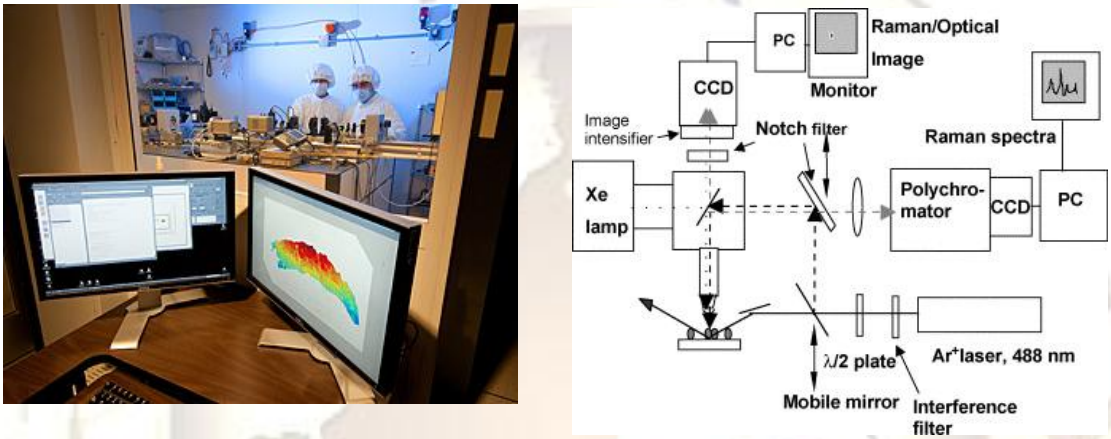


Fig.10: Raman-Optic SM microscope

This includes the extensive application of illumination engineering and optical field control at 193 nm wavelengths. As a part of the NIST research will develop appropriate scatter field test patterns such as those based on optical superstructures applicable to nanotechnology process control to enable high throughput measurements with nanometer resolution. Demonstration of the highest resolution optical measurements are possible using the scatter field concept for dimensional metrology of sub-15 nm sized features with measurement sensitivity significantly better than 1 nm is now a main long term goal [36]. Development of an optical imaging technique have witness a combining between confocal light absorption and scattering spectroscopic to form new metrology technique knowing as (CLASS) microscopy capable of noninvasively determining the dimensions and other physical properties of single subcellular organelles [40].

2.7. Coordinate Measuring Machine (CMM) Technique

Frequent need in progress to examination of human body is required to create new method of diagnosis. The basic metrology tools for coordinate measurements, CMMs are used to evaluate an object through actual dimensional geometrics aspect whose kinematic structure moves in three perpendicular directions (X-, Y- and Z-direction) in Cartesian system. CMM gives the ability to be used in biomedical applications and their accuracy becomes the strongest point in this usage [6, 41]. To diagnose hard tissues properly, one should recognize the external structure of organ such as geometrical parameters and dimension specification. This is a point in which cooperation between coordinate metrology and medicine becomes the most effective. Metrological devices could be used in this area with variety of uses.

2.8. Computed Tomography (CT) Technique

The invention of computed tomography is considered to be the greatest innovation in the field of diagnostic science due to the discovery of X-rays. This cross-sectional imaging technique provides diagnostic radiology with better insight into the pathogenesis of the body, thereby increasing the chances of recovery. Today, CT is one of the most important methods of radiology and mechanical parts diagnosis. It delivers non-superimposed, cross-sectional images of the body, which can show smaller contrast differences than conventional X-ray images. This allows better visualization of specific differently

structured soft-tissue regions, and all different materials for example, which could otherwise not be visualized satisfactorily.

Sequential CT produces a cross-sectional image by scanning a transverse slice of the body from different angular positions while the tube and detector rotate 360° around the patient with the table being stationary as seen in Fig.11. The image is reconstructed from the resulting projection data. If the patient moves during the acquisition, the data obtained from the different angular positions are no longer consistent. The image is degraded by motion artifacts and may be of limited diagnostic value. The CT technique is suitable only to a limited extent for the diagnosis of anatomical regions with automatism functions such as the heart or the lung [42].

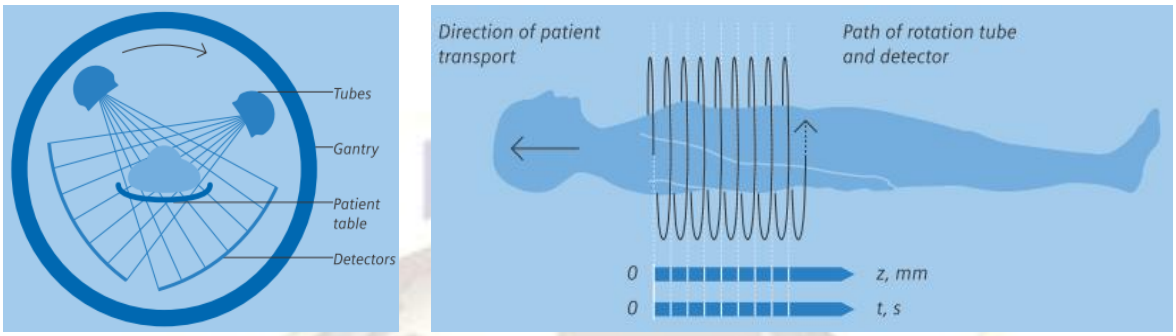


Fig.11: Principle operation of CT technique in medicine

Spiral CT is often referred to as "volume scanning". This implies a clear differentiation from conventional CT and the topographic technique used there. Spiral CT uses a different scanning principle. Unlike in sequential CT, the patient on the table is moved continuously through the scan field in the z-direction while the gantry performs multiple 360° rotations in the same direction. This volume is created from a multitude of 3D picture elements. A CT system comprises several components which include these basic components:

1- The scanning unit the gantry, with tube and detector system as illustrated in Fig.12
2- The object or patient table
3- The image processor for image reconstruction,
4- The console represents the man-machine interface and is designed to be multifunctional control unit for all examination procedures [42].

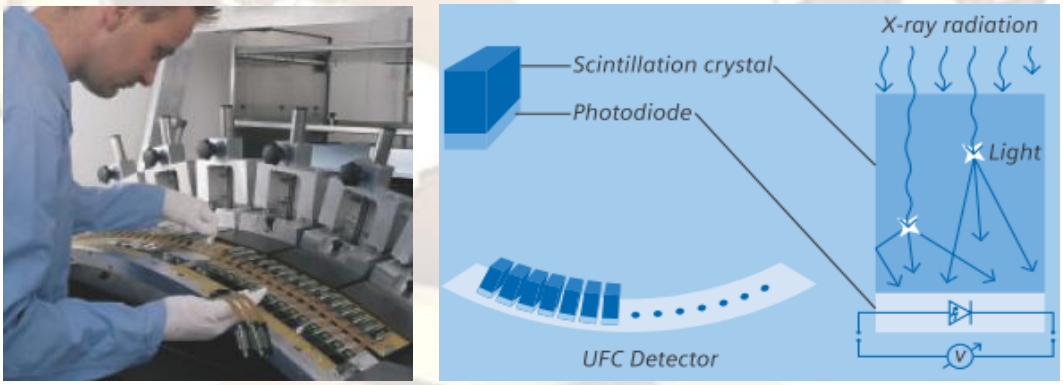


Fig.12: Sample of detector and how it operates.

III. ADVANCED BIOMATERIAL OBJECTS

Advanced materials as an object are a result of truly interdisciplinary efforts and belong to a class of materials that display unusual behaviors which can be harnessed to diverse engineering industries catering to our daily needs (e.g. cell phones, space exploration, medical diagnostics and treatment). Nanotechnology is an emerging engineering discipline that applies methods from nanoscience to create products. The metrological challenges in nanoscience and technology lie in its peculiarity. The laws of physics at this dimension operate in unfamiliar ways defining behavior and imposing constraints on what is possible for design, measure and utilization [6].

Advanced biomaterials have probably the most widely appreciated. Stakes are extremely with high value as such materials to be life savers and others may be used to sustain or improve the quality of life. Examples include stents for keeping the blocked arteries work, genetically engineered organs such as heart valves, eye lens implant or simply a hip

replacement. Of course drugs and advanced diagnostic materials are other classes that need to be mentioned. A new wave of advances in cell biology, chemistry, and materials science is enabling the production of a new generation of smart biomaterials. Drug delivery systems through controlled transport to combat brain cancer, tissue regeneration, polymeric coated stents and many other approaches. Currently, pursue chemical technologies within the framework of reparative medicine include cell-based therapies, artificial organs and engineered living tissues. Nano-reliability measures the ability of a nanoscale product to perform its intended functionality. In the nanoscale, the physical, chemical and biological properties of materials differ in fundamental valuable ways from the properties of individual atoms, molecules or bulk matter [6-8].

IV. SURFACE CHARACTERIZATION OF NANOBIOMATERIAL OBJECTS

Scientific characterizations of nanobiomaterial objects require many different applications using advanced nanometrology techniques such as TEM, SEM, STN, AFM, SPM, CMM and CT techniques.

4.1. TEM Applications

The transmission electron microscopy has important application especially in the carbon nanomaterials. Carbon is perhaps the only element which has an infinite number of allotropes. Some of them can appear very similar to carbon nanofibers and multiwalled carbon nanotubes look similar when observed with scanning electron microscopy. It is almost impossible to distinguish between carbon nanofibers and multiwalled carbon nanotubes unless one observes such materials by TEM. It gives direct insight into the structure of carbon nanomaterials and can help to identify the material / phase correctly. So finally we can say that TEM becomes the most important and most reliable technique for correctly identifying the nature and the geometrical form of carbon nanomaterials as shown in Fig.13 [36]. The samples used for TEM must be very thin usually less than 100 nm, so that many electrons can be transmitted across the specimen. However, some materials such as nanoshells, nanotubes, nanocrystalline powders or small clusters which are used for treatment of cancer and detecting the component responsible for heart attack in heart blood vessels can be directly analyzed by deposition on a TEM grid with a carbon support film [3].

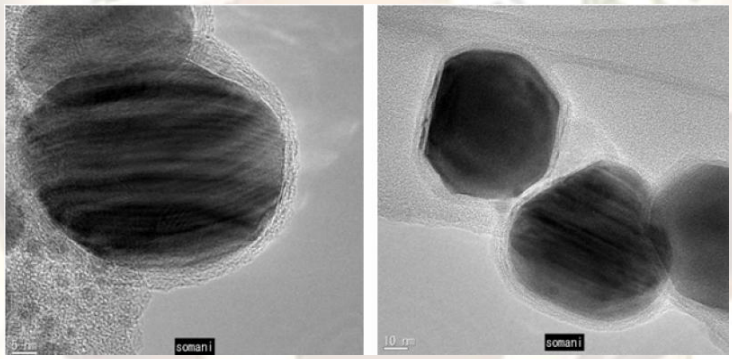


Fig.13: TEM micrograph of carbon nanocapsules encapsulating Co nanoparticle.

TEM have the ability to illustrate the growth mechanism of CNTs as in Fig.14 disclosing the growth mechanism of carbon nanotubes in different stages and time intervals of plasma discharge. Fig.14a depicts a rod like tubes coming out of its carbon mother base which may be considered incomplete growth stage of carbon nanotubes. Fig.14b shows the start of the separation of a CNT from its base after completion of their growth, while Fig.14c exposes a completely separated CNT of which its length and diameter could be assessed [43].

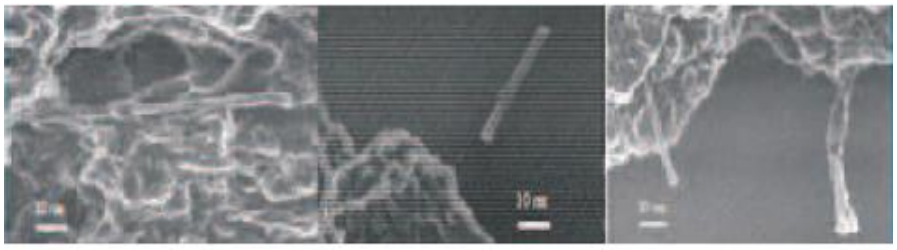


Fig.14: TEM images of CNTs growth mechanism

The HR-TEM is used in biomedical application for analysis of different types of nano-diamond powders on HR TEM (material characterization, the normal distribution of grain size). Nano-Diamond has biological activity where particles have been examined in different fields of medicine in vitro, in vivo and clinical examinations. Nano-diamond powders will be applied in dermatology cosmetology and vessel surgery [21]. This work can observe the conglomerates of nanodiamond crystals and sizes of grains from 2-10 nanometres, see Fig.15.

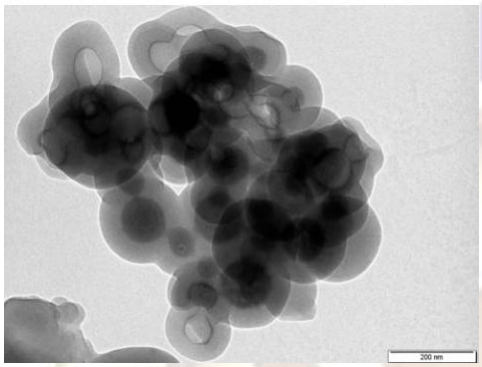


Fig.15: HR TEM image of manufactured nano-diamond particles by microwave/radiofrequency (MW/RF) method

Nano-diamond particles manufactured by microwave radiofrequency (MW/RF) method have bigger grain size (about 150-200 nm) and have round shape. The interesting point is the presence of amorphous phase in grains Fig.16. Nano-diamond particles manufactured by radio frequency plasma assisted by chemical vapour deposition (RF PACVD) method are the biggest among nano-diamonds. The graphite powder carbon control has the patchy structure and the size of grains is less than 1µm as illustrated in Fig.17 [21].

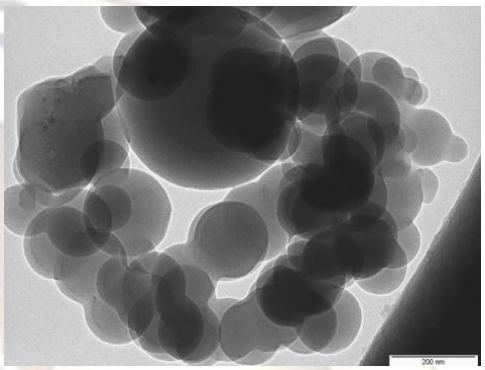


Fig.16: HR TEM image of nano-diamond particles manufactured by MW/RF method

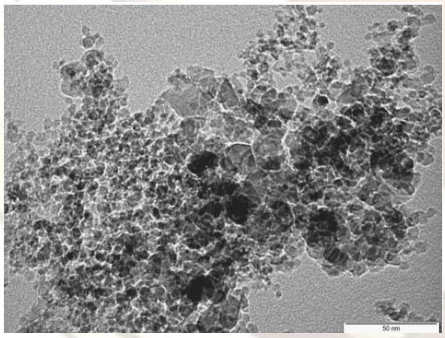


Fig.17: HR-TEM image of nanodiamond particles manufactured by detonation method.

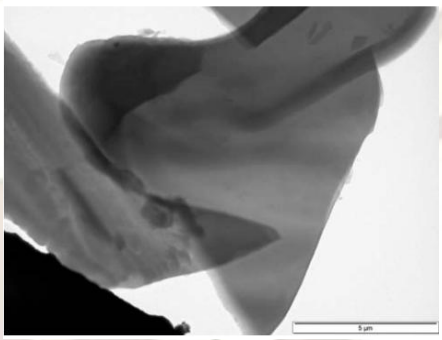


Fig.18: HR TEM image of graphite powder.

The best structure for biocompatibility of human cells is examined in this section by using nanodiamond powder manufactured by detonation method, Fig.18. It can observe the conglomerates of nanodiamond crystals and sizes of grains from 2-10 nanometers. In the other hand, Orlando J. Castejón examined the cerebellar Golgi cells by using TEM to explore Golgi cell's participation in the granular and molecular layers of the cerebellar cortex [21].

4.2. SEM Applications

In hydrated samples addressed by placing a specimen in an environmental chamber with either an electron transparent window or a small aperture for the beam to enter the chamber are examined by SEM. An example of imaging of a pesticide film on skin can be seen in Fig.19.

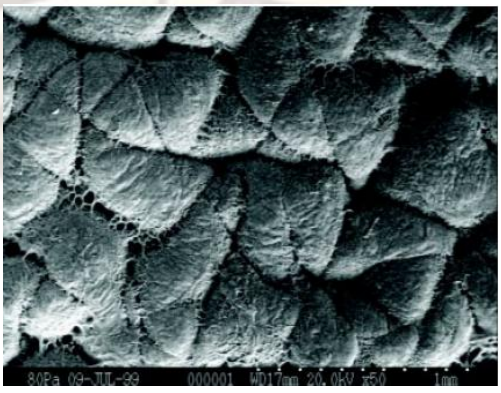
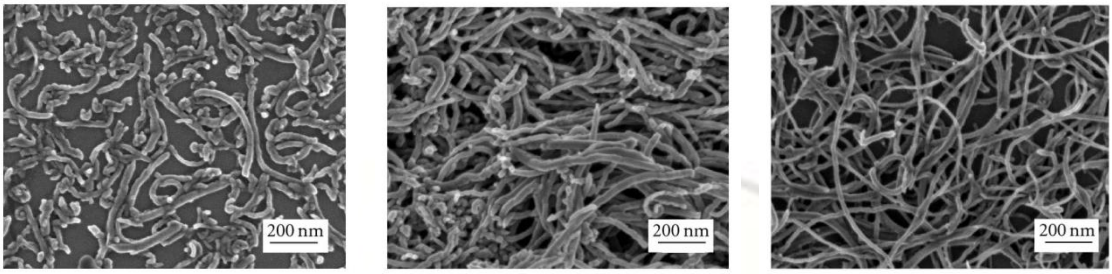


Fig.19: Environmental SEM image of a pesticide film on skin. A hydrated environment was needed in order to maintain the integrity of the pesticide layer and to reduce charging. Bar =1mm [23]

CNTs have recently become the most promising functional materials in nanocomposites. They have been extensively focused on over the past few years due to its unique structural features, amazing properties and for its potential technological applications [44]. SEM observation of as-received MWCNTs Length distribution for carbon nanotubes dispersing in water is very crucial parameter because to a large extent it determines biological effects of carbon nanotubes in water. Detailed information of length distribution is necessary and helpful to deeply understand biological effects induced by carbon nanotubes illustrated in Fig.20 [41].



(a) (b) (c)

Fig.20: SEM images of three kinds of as-received MWCNTs with different average length: (a) 0.5~2 μm, (b) 30 μm, and (c) 50 μm [41].

Blood platelets adhesions have been seen as application on SEM through the surface of any biomaterial strongly depending on the presence and exposure of adhesive proteins such as collagen, fibrinogen, fibronectin and others. Figure 21 shows the SEM of UHMWPE and the UHMWPE–MWCNTs Powders [45]. The micro-morphology in the fracture surface of the UHMWPE/HDPE and the nanocomposites which is carbon nanofibers are presented as shown in Fig.22 using SEM. Fig.23 illustrates example of photos of selected biomaterial surface fragments using SEM. Figure 24 shows the importance of TEM for carbon nanomaterials nanocapsules encapsulating research.

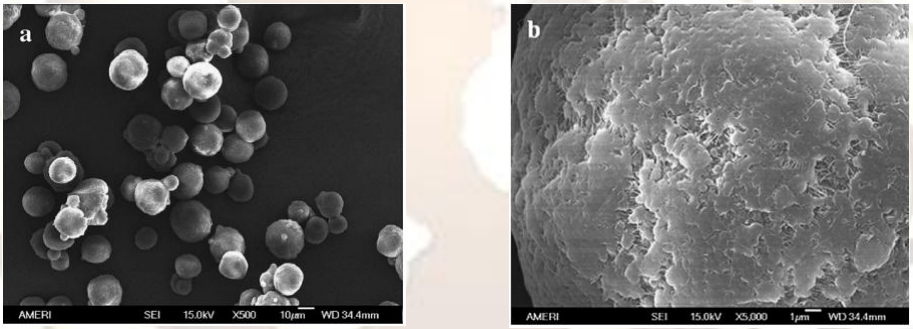
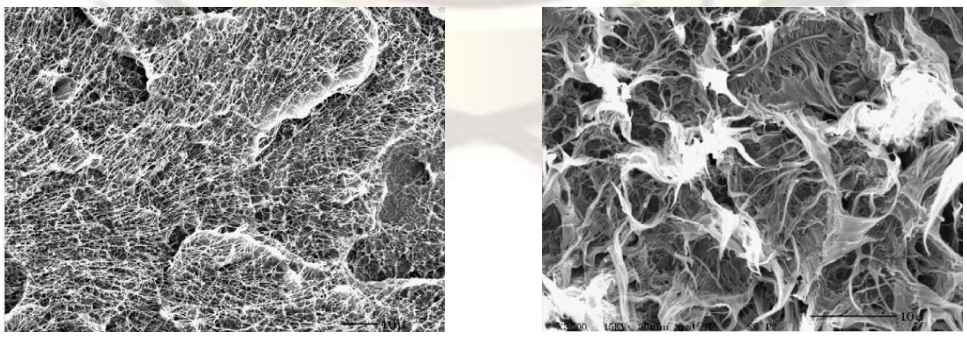


Fig.21: SEM micrographs of (a) UHMWPE Powder and (b) UHMWPE–CNT powder mixture.



(a) (b)

Fig.22: Fracture morphology of (a) UHMWPE/HDPE blend with ratio of 3:7 wt%. (b) UHMWPE/HDPE with 0.5wt% Carbon nanofiber [46].

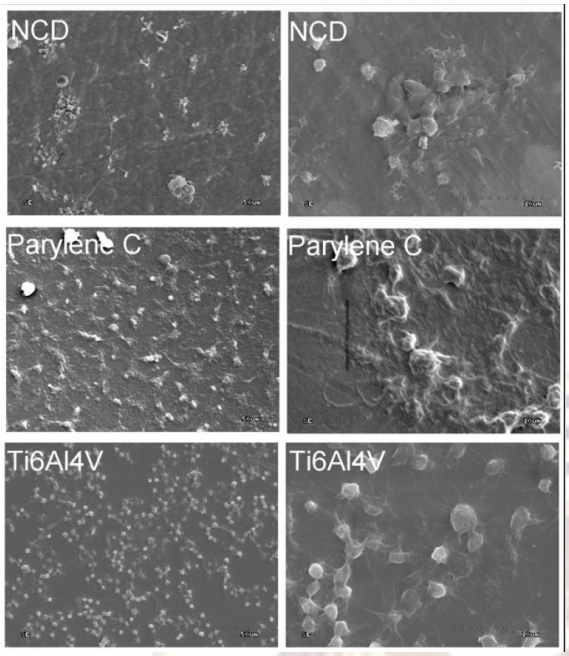
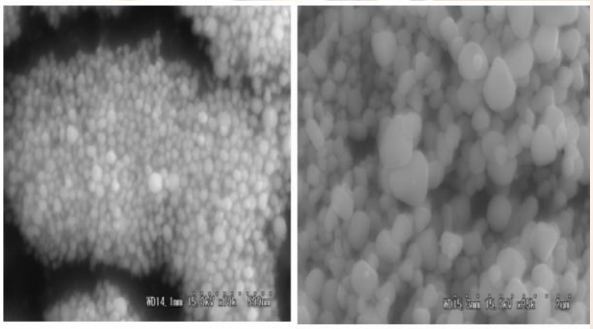


Fig.23: Blood platelet adhesion surfaces observed with SEM [47].



(a) (b)

Fig.24: SEM photograph of carbon nanocapsules encapsulating Co nanoparticles (Note that the appearance looks like metallic nanoparticles and looking at such a picture one can easily get a notion that they are metallic nanoparticles only) [36].

4.3. STM Applications

STM provides a powerful method to detect the surface of conducting and semi-conducting materials. Recently, STM can also be applied in the imaging of insulators, super lattice assemblies and even the manipulation of molecules on surface. More importantly, STM can provide the surface structure and electric property of surface at atomic resolution with a true breakthrough in the development of nano-science. In this sense, the data collected from STM will reflect the local properties even of single molecule and atom. With these valuable measurement data, one could give a deeper understanding of structure-property relations in nanomaterials [28]. Figure 25 provides an image of RNA by using STM image of retinoic acid on a graphite substrate.

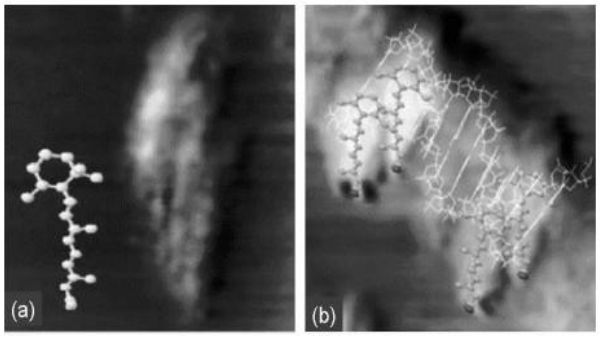


Fig.25: Comparing molecular model showing the aliphatic ring head and polymeric tail. (b) STM image of retinoic acid binding to t-RNA with molecular model overlay [43].

4.4. AFM Applications

It can be used in many different areas to analyze different kinds of samples such as semiconductors, polymers, nanoparticles, biotechnology and cells amongst others. The most common application of AFM is for morphological studies in order to attain an understanding of the topography of the sample. Since it is common for the material to be in solution, it can provide a lot of information about the particles being studied such as particle size, surface area, electrical properties and chemical composition. Certain tips are capable of determining the principal of mechanical, magnetic and electrical properties of the material. For example in magnetic force microscopy (MFM), the probe has a magnetic coating that senses magnetic, electrostatic and atomic interactions with the surface. This type of scanning can be performed in static or dynamic mode and depicts the magnetic structure of the surface [18]. Over the past decade, AFM had provided mechanistic insights into the molecular level interactions that occur at the biomaterial interface. The molecular processes have contributed to the advancement of the AFM as a state-of-the-art research instrument. These articles examine some applicability of the AFM to the study of biomaterials and cell/molecular interactions [48-49], to characterize the surface of the bone scaffold biomaterial, polycaprolactone (PCL), by scanning with the AFM and measuring adhesion forces between fibronectin-coated PCL and human integrin, producing 3D images with features ranging from nanometer to micrmeter dimensions. Finally, by AFM, measuring forces on the order of nano-Newton (nN) is done [50]. The AFM is demonstrated as a detector for long chain polymers and provides very sensitive detection of polymeric strands using the force spectroscopy mode of operation [51]. To design polymeric biomaterials with specific surface properties it is necessary to develop surface analytical techniques that can accurately characterize these properties. The article has aimed to investigate the potential contribution of the advanced AFM to this characterization [52]. Bio-degradable polymer

nanofiber is applying in Fig.26 [53].

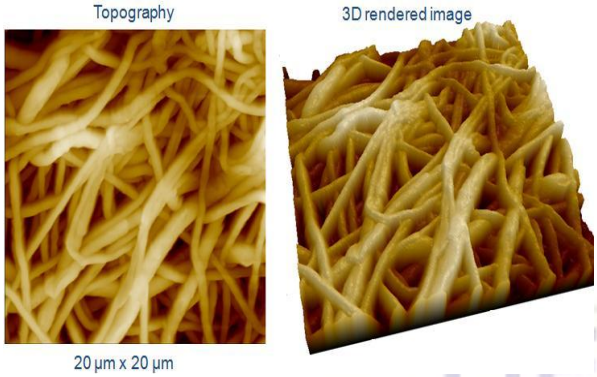
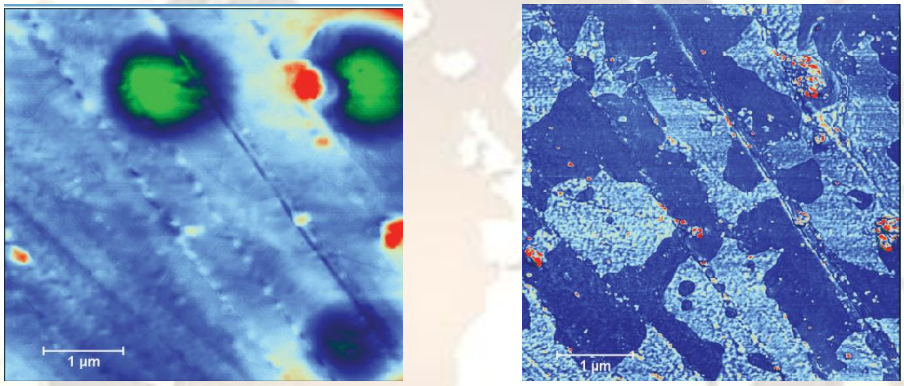


Fig.26: Applying of AFM at polymer nanofiber [53].

Atomic Force Microscopy works equally well on insulators or conductors in Imaging Hydrogel Coatings so it is important for the manufacturer to understand how the coating behaves when applied to a surface. The sample must be completely dry since water is the main constituent 80% of hydrogels, and working in a vacuum presents serious obstacles for both dry and wet samples. AFM analysis generates high resolution topographic information not readily available from other techniques [54]. As a result, this application is explained below. Figure 27(a) shows the surface topography of a 5mm x 5mm area of a polyurethane tube coated with a lubricious hydrogel. The colors indicate the height of the surface -dark blue being low and red being high. The height (Z) range is 100 nanometers while Fig.27(b) indicates a phase image of the same area and was acquired simultaneously showing that the coating has areas with different physical characteristics.



(a) (b)

Fig.27: AFM images for: (a) surface topography, (b) phase image

These different areas are not readily apparent in the height image of the tube after the tube has been moistened; however, the surface of the tube becomes quite uniform, as seen in Fig.28. This indicates that the addition of water has dramatically changed the characteristics of the coating.

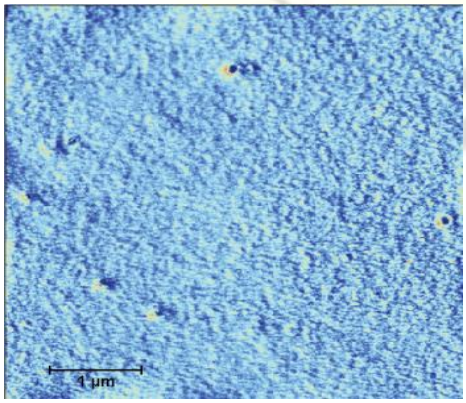


Fig.28: Phase image, tubing after being moistened [54]

In dental composite application, the characteristics of biomaterials are essential at the first step for understanding of their performance. Special interest is the characterization of internal and external interfaces of biomaterials as they determine the biomaterial's mechanical performance and the interaction. Figure 29 (a and b) show result from a fractographic AFM study of light polymerized microfilld dental composite. Height and cantilever oscillation amplitude data obtained in tapping mode were recorded. The composite contains 40% silicon dioxide fillers with a grain size of 0.02-0.07µm (manufacture data) [48].

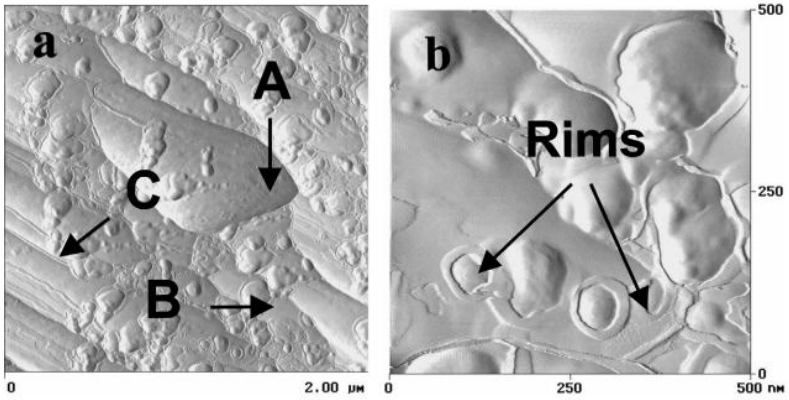


Fig.29: AFM amplitude images of fractured dental composite surfaces .Resin matrix (A) and filler particles (B) can be seen in (a). Fractured lines (C) separate different surface areas. Most filler particles can be seen in (b).These rims are likely to originate from the silane compatibility agents used to bind filler particles to resin. The width of the rims is a few 10 nm [48].

Figure 30 shows AFM images for two different titanium implant surface when interpreting the surface roughness values of biomaterials with several points [48]. Another application of AFM in biomedical fields is given in Fig.31. One of the most active areas of the application of AFM in biomaterials science is mineralized tissue research, where AFM image of prismatic and prismatic human enamel is shown in Fig.32. Figure 33 shows good resin penetration and biomaterial bonding for human dentin. Characterization of the shape, size and properties of such structures requires specialist techniques such as ultra-low force AFM. An example of an AFM image of a DNA tetrahedron is shown in Fig.34 [11].

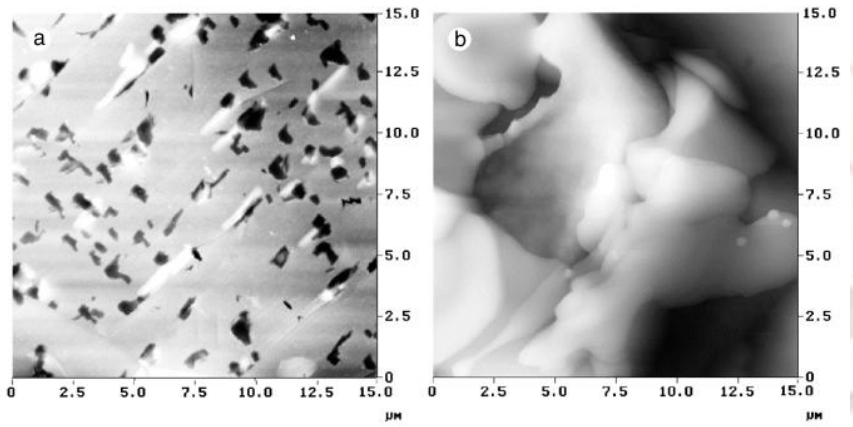


Fig.30: Mechanically polished titanium implant surface (AFM tapping mode in air z-rang 2.50µm) [48].

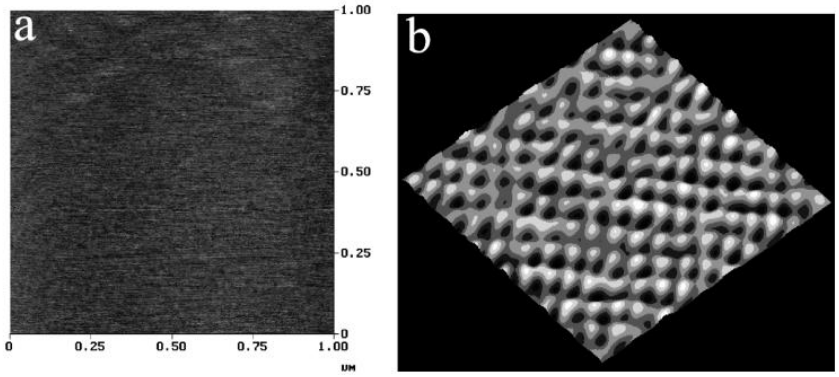


Fig.31 AFM images of ultra-flat TiO_2 sample surface produced by a template stripping method after. (a) High resolution imaging of the TiO_2 samples surfaces (b) shows atomic resolution of the TiO_2 is frequently used in implants and the samples presented here are suitable to obtain molecular resolution of absorbed bimolecules with AFM.

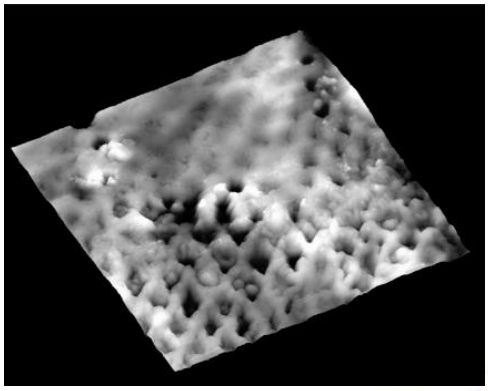


Fig.32: Native human enamel surfaces imagined with tapping mode AFM [48].

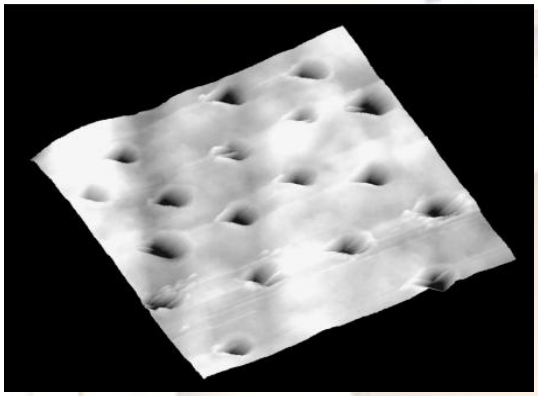


Fig.33: AFM image of human dentine treated [48]

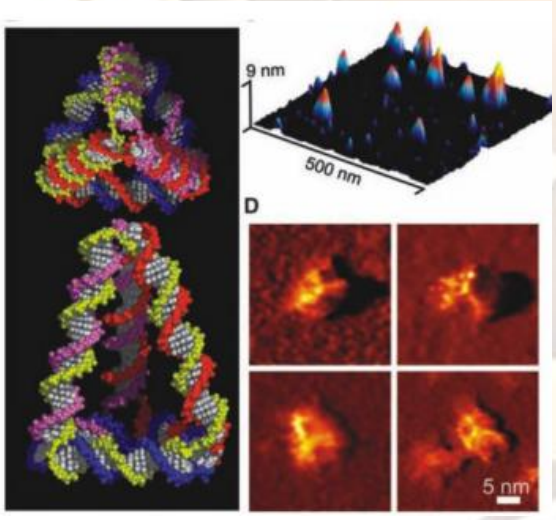


Fig.34: Schematic image of DNA tetrahedron prepared by self-assembly method, AFM topography image of such structures showing the shape and size of individual structures [11].

The primary attraction to the AFM is its ability to image insulating surfaces at high resolution in fluid. Imaging samples in a hydrated state with an AFM is commonly performed by enclosing the sample and probe in a fluid environment as illustrated in Fig.35 [24]. The tapping Mode of AFM is used in living human vascular endothelial cells, see Fig.36.

Also, it is used in fixing soft bio-mimetic nanoparticles on surfaces without distorting or denaturing them so that they can be examined with AFM. Medical applications range from imaging contrast agents to therapeutic cancer treatments. Carbon nanotubes, fuel cell membranes and cellulose nanocrystals (CNCs) are among the challenging materials for which advanced AFM techniques are being investigated [55]. The rapid progress of interest in carbon nanotubes research shows that AFM is also an excellent tool for single nanotube characterization and treatment. Characterization of MWNT gives a new wider approach to the structure and quality characterization carbon nanotubes.

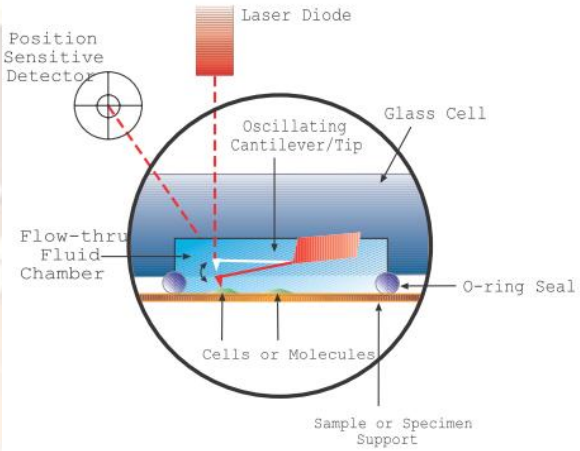


Fig.35: Fluid cell for an AFM which allows imaging in an enclosed, liquid environment [24].

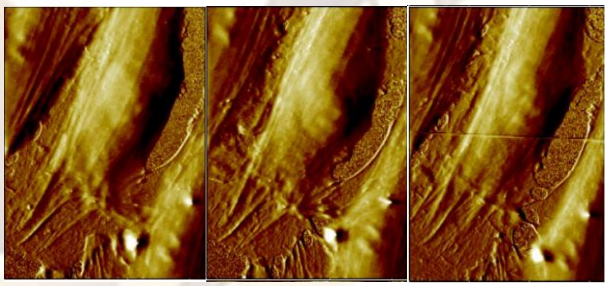


Fig.36: Tapping Mode of AFM [24].

4.5. Confical Microscopy Applications

Confocal provides information on identity size, stereo-structure, time-change, substance diffusion, and concentration of fluorescent-labeled substances. In the pharmaceutical industry, confocal microscopy is now widely applied tool for studying the cellular effects of drug candidates. For cellular imaging, confocal optics provides a significant improvement in spatial resolution and data quantity. Confocal microscopy is applied in neurobiology for detecting microstructures and activities within neurons see Fig.37. The technique is also used in clinics for disease diagnoses in tracing pathological

changes and in studies of angiogenesis under several conditions. Furthermore, researchers in genetics use confocal microscopy to trace the expression of genetically encoded fluorescent proteins. The field of live-cell imaging has also greatly benefited from applications of confocal microscopy. Future developments in this field will be of great interest and benefit to both biotechnological and medical research [35].

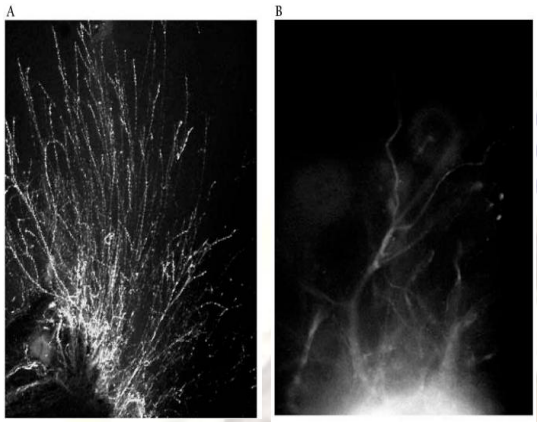


Fig.37: Comparison of wide-field epi-fluorescence and scanning confocal images of neurite out-growth

The idea of confocal imaging implies that the volume of material has to be scanned layer by layer. This process takes time. Confocal microscopy has been widely used in research and therapies in the clinical treatment of disease. In addition to the applications in cancer research and Alzheimer's studies mentioned previously, it is reported that the technique is widely used in ophthalmology, angiogenesis, gynecology, and gastrointestinal systems where confocal microscopy allows ophthalmic clinicians and researchers to visualize living tissues at greatly increased resolutions [35]. For pharmaceutical applications: it has also been reported that confocal microscopy is also used by pharmaceutical companies for biochemical screening and drug development. Tumor cells exposed to quantum dots are illustrated in Fig.38 using confocal microscopy [56].

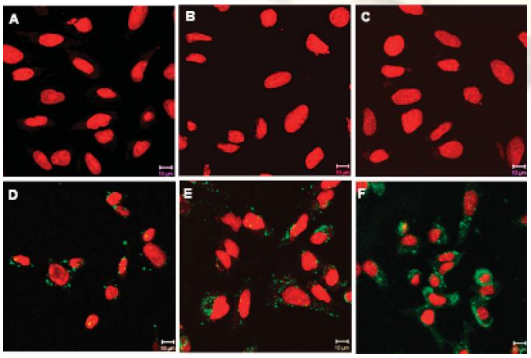


Fig.38: Sizes for 3 hours: a) 40 nm; b) 80 nm; c) 145 nm; d) 40 nm; e) 80 nm; and f) 145 nm by confocal laser [56].

Intracellular nano-flares on a human breast cancer cell line is shown after transfection with nano-flare particles in Fig.39, specifically targeting the surviving mRNA (messenger RNA) sequence known to be expressed [57].

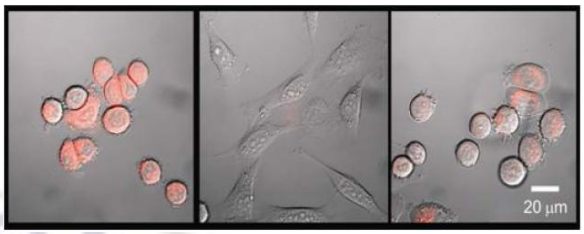


Fig.39: On the left, bright fluorescence is observed as the nano-flare sequence is complementary to the targeted surviving mRNA sequence. On the right, a control scrambled nano-flare sequence was added and minimal fluorescence is observed. The middle panel demonstrates the lack of surviving nano-flare fluorescence following transfection in a cell line that does not express surviving [57].

4.6. Raman Scattering Applications

The development of a sensitive and high throughput Raman spectroscopy provides a wide range of applications. An experimental study of brain tumors are classified according to their primary cells and to their malignancy. In Fig.40 (A), detections of tumor cells within white and gray matter of normal brain tissue was facilitated by Raman spectrum. While Fig.40(B), shows an extended tumor approximately 240×240 μm^2 was identified in the Raman map. Figure 41 shows the Broadband CARS image of tertiary polymer blend [color coded: polyethylene terephthalate (PET) in blue, polymethyl methacrylate (PMMA) in blue and polystyrene (PS) in red], and examples of spectra obtained at each pixel (right) [58].

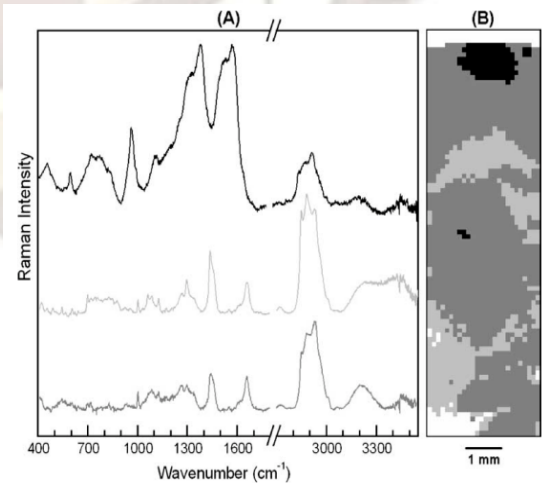


Fig.40: Raman spectrum detection brain cancer [40].

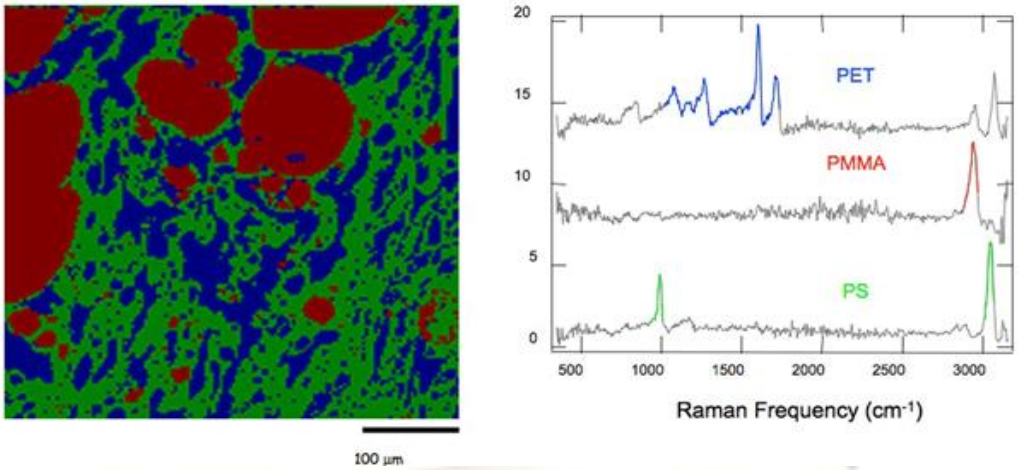


Fig.41: NIST Raman broadband CARS image of tertiary polymer blend

4.7. CMM Applications

For a long-term successful enhanced biocompatibility have providing quality criteria. CMM machine gives possibility to measure objects with uncertainty less than 1µm. It is also possible to scan the measured surface by using scanning probe head [59]. Figure 42 shows a clear practical application of CMM in biomedicine.

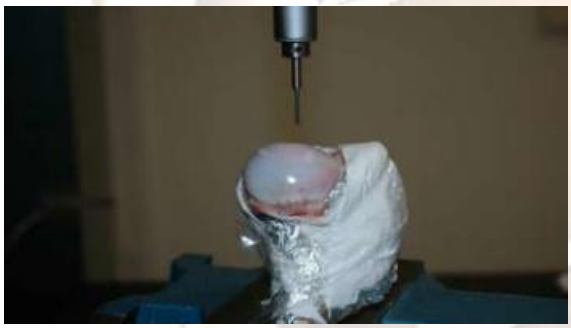


Fig.42: Measurement of human knee-joint

Fig.43: Inspection of artificial heart pump using CMM [60]

Contribution of surface form and geometrical position are absolute necessary in object as shown in Fig.43 for dimensional conformance measurement which developed by CMM inspection and metrology solutions. Clinical experience require quality characteristics to be demonstrated by analysis and evaluation of dental implants dimension and geometrical form through CMM machine as seen in Fig.44 [61].

Fig.44: The original tooth while CMM [61-62]

4.8. CT Technique Applications

Computed tomography technique play an important role as a coordinate diagnostic tool for hidden objects, especially for mechanical engineering objects, metallurgy and oncology applications. CT application has recently been broadened to include dimensional metrology in industry [63-64]. Figure 45 shows better diagnosis of both lungs, both kidneys and vertebral column bone using CT technique. It is clear that there is soft tissue mass with dimensions 5×6×5 cm of the left kidney.

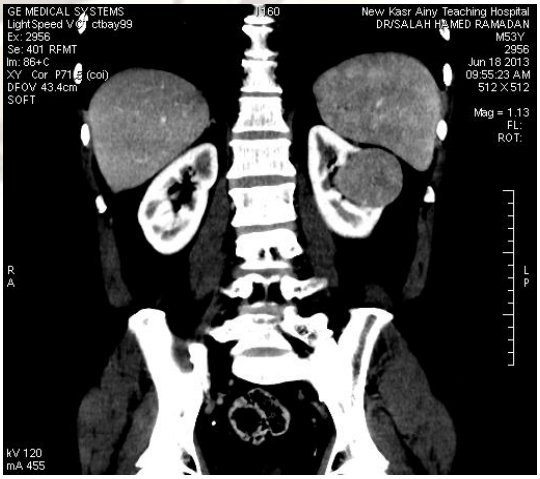


Fig.45: Longitudinal contrast-enhanced CT technique shows lesion of left kidney.

V. COMPARISON BETWEEN ADVANCED METROLOGY TECHNIQUES

Nanometrology techniques open the door to imaging nanomedicine applications [65]. Surface properties can have an enormous effect on the success or failure of variety of characterization techniques in the evaluation of biomaterial surfaces. It should be noted that the use of different microscopic techniques might give rise to a different view of the surfaces obtained. However a comparison shown between SEM, TEM and AFM images of the same polyamide polymeric material [66] will be conducted with respect to 3 factors: (1) Surface Structure (2) Composition, and (3) Environment [24].

5.1. SEM & TEM

They are commonly used for studying both the surface morphology of and the cellular response to biomaterials. SEM sample preparation involves fixation (if proteins, cells, or tissue are present), followed by drying, attachment to a metallic stub, and then coating with a metal prior to data collection. TEM sample preparation involves fixation (if proteins, cells, or tissue are present), processing, embedding and sectioning [66]. TEM requires extremely thin specimens for imaging; however, the SEM has lower magnifications. Although both SEM and TEM use an electron beam, the image is formed very differently and users should be aware of when each microscope is advantageous [24]. The electron microscope clearly has the potential to have a huge impact in this emerging area of research because of its unique capacity to determine atomic structures with very high accuracy on a routine basis [67].

5.2. AFM & STM

It's interesting to compare AFM and STM. In some cases the resolution of STM is better than AFM because of the exponential dependence of the tunneling current on distance. The force-distance dependence in AFM is much more complex when characteristics such as tip shape and contact force are considered. STM is generally applicable only to conducting samples while AFM is applied to both conductors and insulators. In terms of versatility, needless to say, the AFM wins. Furthermore, the AFM offers the advantage that the writing voltage and tip-to-substrate spacing can be controlled independently, whereas with STM the two parameters are integrally linked [67]. AFM images can be acquired under vacuum, air, or liquid conditions. The ability to image polymeric materials within an aqueous environment is extremely useful in the biomaterials field. It is possible to visualize individual plasma protein molecules under aqueous environments using phase imaging AFM .Although AFM is proving to be an extremely useful technique in providing a 3D visualization of the biomaterial surfaces being studied the time required is dependent on such factors as scan size and scan rate to obtain quality images to be significant [66].

5.3. AFM & SEM

AFMs probe is the simple and make measurements in three dimensions, *x*, *y*, and *z* (normal to the sample surface), thus enabling the presentation of 3D images of a sample surface. This provides a great advantage over any microscope available previously. With good samples (clean, with no excessively large surface features) [12]. Compared with Scanning Electron Microscope, AFM provides extraordinary topographic contrast direct height measurements and unsecured views of surface features (no coating is necessary) [68].

5.4. AFM & TEM

Compared with Transmission Electron Microscopes, three dimensional AFM images are obtained without expensive sample preparation and yield far more complete information than the two dimensional profiles available from cross-sectioned samples [66].

5.5. Morphology Parameters

The most common set of morphological parameters- using different metrology techniques- is presented in Table 5. It clears that, parameters involving measurements of the third dimension such as height, surface roughness and volume are possible only with AFM [69]. The ability to visualize and directly measure dimensions of a few nanometers is a necessity in nanotechnology. There are few particle analysis techniques capable of delivering morphological information below 100 nm. In fact, AFM is a non-intrusive technique with resolution greater than or comparable to that of SEM and TEM techniques.

Table 5: Common set of morphological parameters available for measurement

Morphologica parameters	Metrological techniques			
	Optics	TEM	SEM	AFM
Size, radii, length; width	Yes	Yes	Yes	Yes
Aspect ratio	Yes	Yes	Yes	Yes
Height	No	No	No	Yes
Perimeter	Yes	Yes	Yes	Yes
Projected area	Yes	Yes	Yes	Yes
Surface roughness	No	No	No	Yes
Volume	No	No	No	Yes

VI. TIME AND COST FOR MEASUREMENTS

The time required for making a measurement with the AFM image is typically less than SEM and TEM, while the amount of time required to get meaningful images is similar. This is

because the SEM and TEM techniques are often require substantial time to prepare a sample. But with the AFM technique, little or no sample preparation is required [32]. In comparison with an optical microscope and the SEM, TEM and AFM is more difficult to use than the optical microscope and easier to use than the SEM or TEM. Figure 46 compares the relative time and cost for optical, AFM, SEM and TEM techniques. Lastly, an optical microscope requires the least amount of laboratory space, while the SEM and TEM require the most area of laboratory space. AFM lies in the middle of the other two. Finally, in comparison with an optical profiler, the AFM is only more difficult to use. This is because the optical profiler does not need any adjustments. However, the AFM technique requires adjustment of the scan speed and the feedback control parameters.

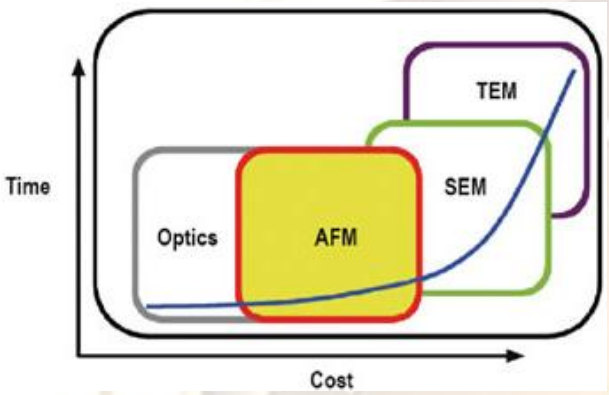


Fig.46: Comparison chart of cost and time for measurements using optical, AFM, SEM and TEM techniques

VII. CONCLUSIONS

In this paper the authors have provided an overview of most recent advanced coordinate metrology techniques and its development allows measurements and examination of objects in nanomedicine. The choice of biomaterial is of course determined by the medical application for which it is intended to fully biocompatible and biotolerant, commonly used in nanobiomaterials objects characterization as well as some discussion of emerging methods. Moreover, focus on how these techniques help to use in nanomedicine and cover the properties about each electron microscopy and the area of applications. Briefly, the following conclusions could be drawn:

1- SEM and TEM techniques are commonly used for study the surface morphology and the cellular response to engineered biomaterials objects.
2- It was found that the AFM technique has many updated applications compared to the other metrology techniques in the nanomedicine and in different object applications.
3- CT technique is the new addition to advanced coordinate metrology; this is due to unique property to acquire the complete volume of objects in the hidden complex geometrical macrostructure to be suitable in 3D.
4- CT 3D nano-scale imaging technique suggests the potential for the development of multifunctional nanoparticles that facilitate accurate realization of individualized cancer therapy. Almost all types have been evaluated for their suitability as multifunctional nanoparticles that can be applied for simultaneous in vivo imaging and object treatment of tumors and organ elements.
5- AFM is an excellent technique used to characterize structural properties of nanomaterials, specially this technique has less time for measurement and fixed costs.
6- Nanoparticals and CNTs could be considered as providing the original seeds for the ongoing nanotechnology revolution in all applications because the preferred characterization is offered by recent progress of nanometrology techniques.

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