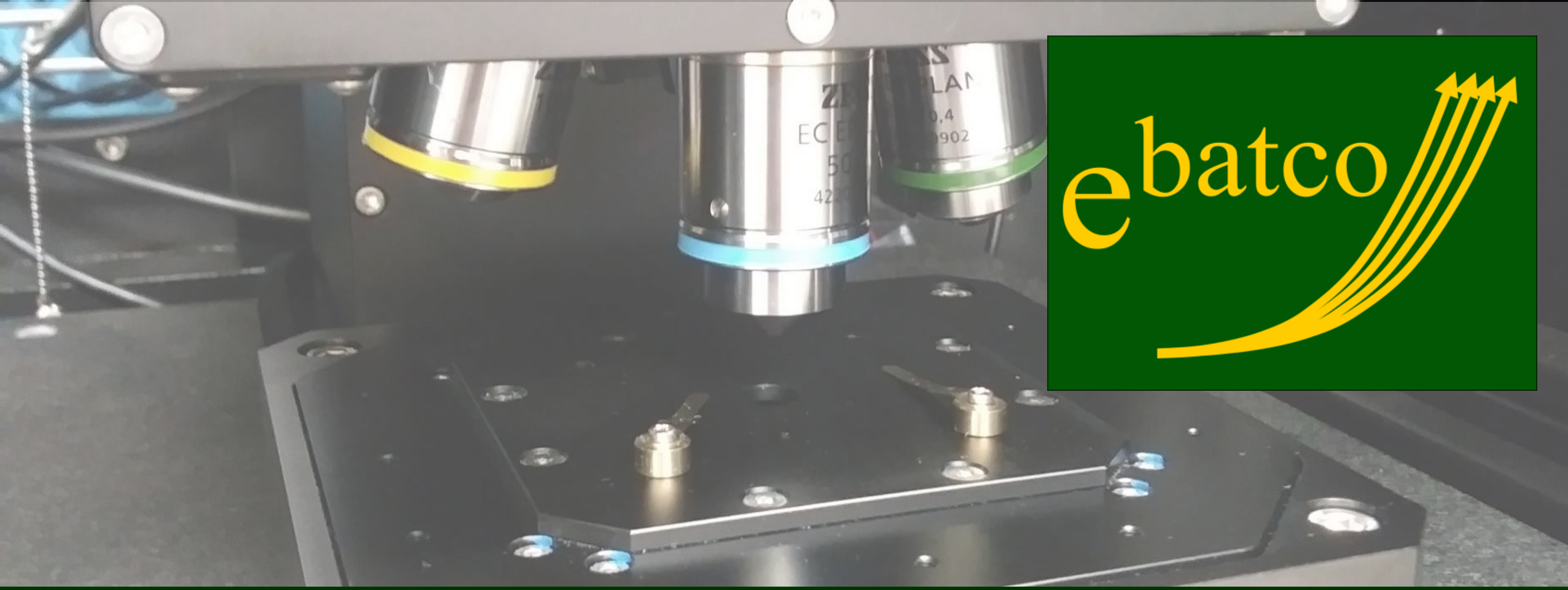

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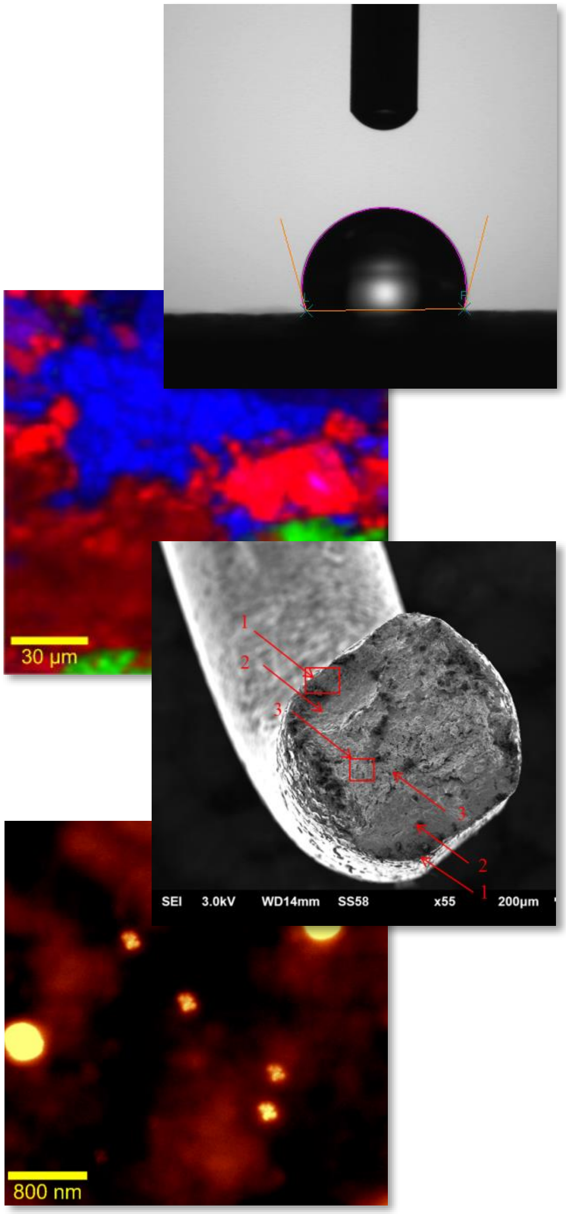

Medical Device Analysis Guide

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Introduction

From inception to market, the process of developing medical devices can be an arduous, yet exciting, experience. Ensuring you have a quality, certified testing lab at your disposal ensures you can respond timely and accurately to both the expected and unpredictable demands of the development process. Having provided the medical device community with over 10 years of support, Ebatco is your choice to streamline your development process. In addition to obtaining ISO 17025 certification, we consistently strive to improve the quality of our offerings through the acquisition of instruments, standards, and novel analysis methods.

There are six prominent areas in which Ebatco serves the medical device community, running the gamut from the production line to after-market litigation: materials testing, process optimization, quality assurance, failure analysis, regulatory filing, and litigation/IP support. The following document explains some common cases that have arisen in the past associated with each testing area to provide you with an illustration of the type of work we do as it relates to the medical device community.

Materials Testing

Five distinct suites of tests are available at Ebatco to characterize any aspect of your medical device: Surface Interface Analysis, Chemical Analysis, Mechanical Analysis, Thermal Analysis, and Particle Sizing. The suites and the associated tools are described in Table 1.

The Chemical Analysis suite offers powerful and rapid analysis of surface contamination, molecular orientation of coatings, grain size and arrangement, active pharmaceutical ingredient (API) and excipient characterization, drug polymorphism, degree of crystallinity, failure analysis, and a host of others.

As the only ISO-certified nano indentation analysis lab in the USA, Ebatco's mechanical analysis offerings are uniquely situation to deliver top-quality and high resolution characterization data, providing you with information regarding material hardness, failure analysis, elasticity, modulus mapping, and nano DMA.

The Thermal Analysis suite provides customers with glass transition temperatures, moisture content, stability of biomaterials, contamination, humidity effects, and coefficients of thermal expansion.

Our Particle Sizing offerings are vital to examining particle runoff, evaluating sanitation protocols, contamination, and failure analysis.

The Surface/Interface suite of testing provides you with information pertinent to zeta potential, surface charging, water contact angles, hydrophobicity, wettability, coating adhesion, pore size, and friction and wear.

Table 1. The Full Suite of Ebatco Analysis Tools and Analytical Tests

Suite	Tools and Tests
Mechanical Analysis	Nanoindentation, Microindentation, DMA, TMA, Young's modulus, glass transitions, coefficient of thermal expansion (CTE),
Chemical Analysis	FTIR microscopy, Raman microscopy, SEM/EDX, TGA/DSC, XRD, AFM
Surface/Interface Analysis	Microcontact Angle, surface free energy, surface tension, interfacial tension, reciprocating wear, pore sizing, Zeta potential, scratch testing, friction, high-load scratch, nanoscratch, microscratch,
Thermal Analysis	Thermogravimetric Analysis (TGA), glass transitions, Differential Scanning Calorimetry (DSC), enthalpy of melting, mass loss, evaporation kinetics
Particle Analysis	Dynamic Light Scattering (DLS), Particle Counting, laser diffraction, Zeta potential,

Failure Analysis and Process Optimization

Medical devices can undergo failure at any stage of their development and application, and optimization of the device is critical. Because of Ebatco's unique combination of mechanical, chemical, and thermal analysis characterization instrumentation, we are well-suited and experienced in characterizing failures and helping you improve your process optimization.

Case Study #1

PTFE coated stainless steel guide wires are popular in many medical applications. PTFE coatings are applied to the wire surface for smooth surface finish, reduced friction, increased lubricity and durability of the guide wire. The PTFE coating adhesion to the guide wire is critical not only for the desired functionalities but also for the health and safety of the patient for whom the guide wire is to be used. An undesired issue would be flaking of the coating material due to adhesion problems, which could lead to blockage of a passage or clogging of blood vessels. Figure 1 is an SEM image of a PTFE coated stainless steel guide wire after scratch test along with the EDS hypermap that is used to confirm that the scratch has indeed passed through the coating and reached the underlying substrate.

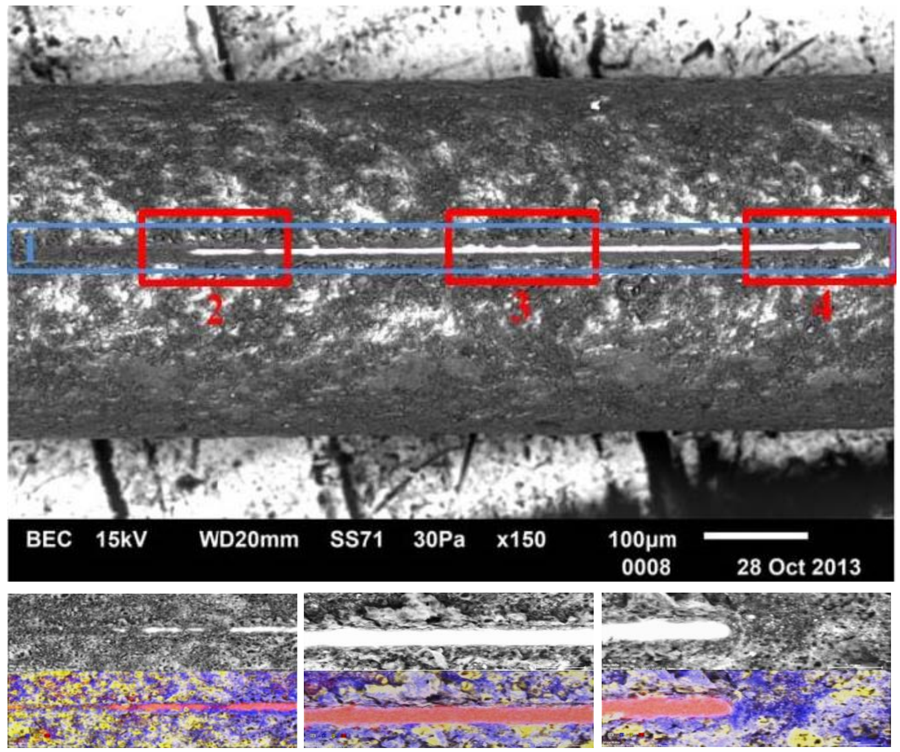

Figure 1. Top: SEM image of a scratch test performed on a steel wire. Bottom: EDS map of different elements exposed during the scratch test at each of the three zones.

Case Study #2

Figure 2 illustrates an SEM image of a steel wire failure. Bending of the wire back and forth has caused both sides of the wire to undergo compression and tension forces, and the final wire rupture.

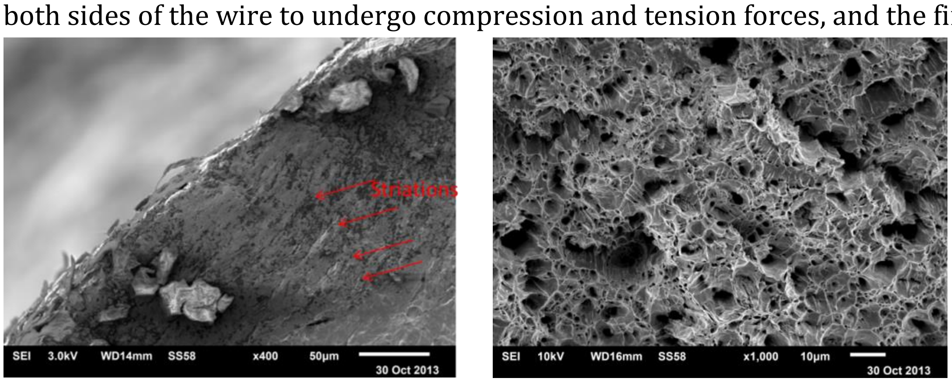

Figure 2. SEM image of a fractured steel wire (left). The areas of striations are viewed at higher magnifications (right).

Figure 2 shows the area close to the crack initiation region. In this image, the striations as typical fatigue characteristics caused by crack propagation can be easily seen. The image below at right illustrates typical dimple structures from ductile fracture in the final fracture region. The dimples are formed due to high local plastic deformation at final rupture of the wire.

Quality Assurance

Maintaining process and product consistency ensures your customers receive the material you intended. For over 10 years, Ebatco has delivered unparalleled support to the medical device industry working with catheters, drug delivery balloons, pharmaceuticals, implants, leads, and pumps.

Case Study #3

Raman microscopy can be used to quantitate the amounts of substances present in a pharmaceutical tablet. To determine the relative quantities of each of the active pharmaceutical ingredients (APIs: acetaminophen, aspirin, and caffeine) present in the pain relief tablet, 15 area maps were generated. Each area map covered an area of 150 µm x 150 µm at 75 pixels x 75 pixels (5625 total pixels each), and the integration time was 74 ms. Each scan took approximately 8 minutes, and the total acquisition time for all 15 scans was 120 minutes. The percentage of each API for each individual area map is shown in Figure 3 (bottom, left) along with the cumulative running average of each API (bottom, right). The relative amounts of acetaminophen, aspirin, and caffeine were determined to be 42 % ± 2 %, 45 % ± 2 %, 11 % ± 1 %, respectively. These values agree well with the packaging label, which indicated the relative amount of each API is 44 %, 44 %, 12 %, respectively.

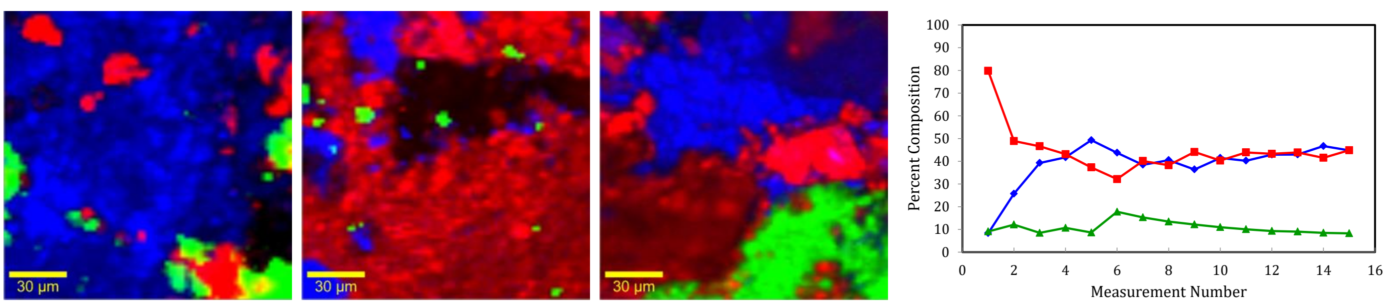

Figure 3. Three false color Raman images (left) show the locations of three APIs. The plot (right) shows how the relative amount of each API can be calculated by obtaining multiple Raman images.

Case Study #4

Fracture toughness is a measure of the material's ability to resist crack propagation and fracture under stress. Commonly used methods for evaluating fracture toughness of materials include bending, tension and impact tests of a specimen with a sharp crack or a defined notch. As regulated and recommended by many ASTM and international testing standards, these methods require the specimen with sufficient thickness and dimensions to ensure measurement validity. In many industrial and technical applications that involve small volume of materials, however, these requirements could not be practically met, for example in thin films, coatings, welds and miniaturized devices.

The unmet needs by the conventional fracture toughness measurement methods have offered an excellent opportunity for the nanoindentation based techniques that are developed for mechanical characterization of small volume materials at nanoscale. Benefited from the established model and in-situ scanning probe microscopy (SPM) imaging capability, fracture toughness measurement via nanoindentation has become a preferred technique for in-situ and small-volume fracture behavior study of materials and many types of medical devices.

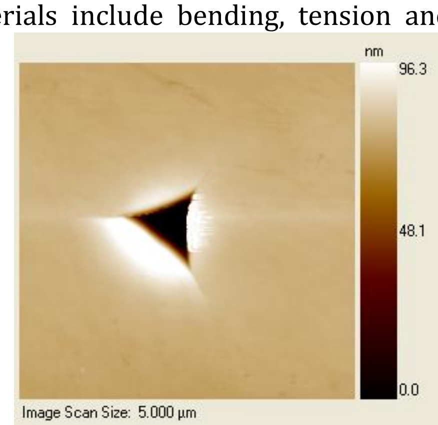

Figure 4. An indent is used to fracture the surface along the vertices of the indent.

Regulatory Filing

Adherence to regulatory guidelines can quickly become a time consuming and stressful experience. Ebatco closely works with many clients in the medical device industry to help align their products to meet the demands of the FDA or other regulatory agency.

Case Study #5

Diamond-Like Carbon (DLC) coatings are frequently used on parts in high performance applications to prevent surface damage or reduce friction of moving parts. DLC coatings can be applied to almost any material that is compatible with vacuum environments and have many applications including electronics, automobiles, tools, shaving razors, and biomedical implants. The hardness and strength of the coating can vary greatly depending on how it is deposited and its intended applications. Due to this high variability, characterizing the properties of such coatings can provide very useful information for the preparation process optimization as well as performance evaluation.

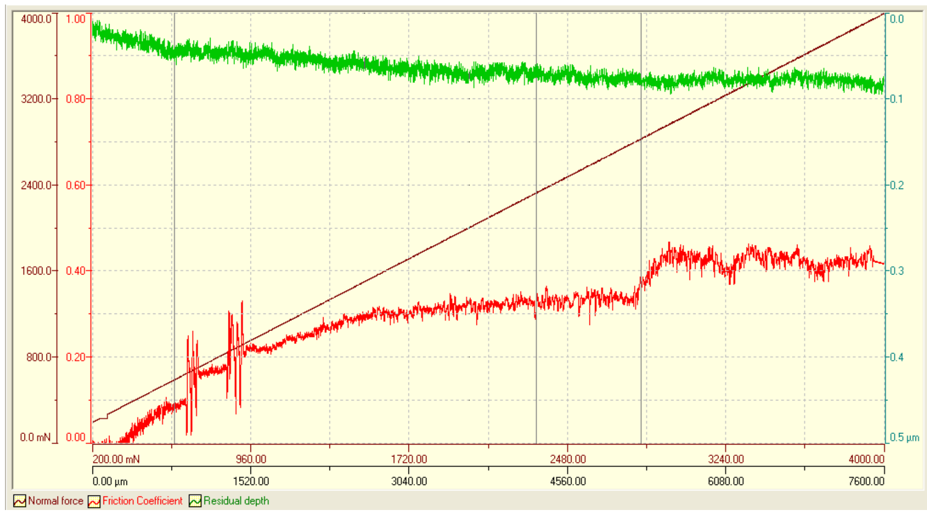

Figure 5. Scratch test results of a DLC coating. Critical loads of failure are indicated by the vertical lines.

Figure 5 illustrates one method for characterizing the properties of DLC coatings is scratch testing. In this method, a diamond stylus that is subjected to an increasing normal force is drawn across the coating surface. At some point, the coating will fail due to increased normal and tangential stresses applied by the moving diamond stylus. The normal forces applied to the scratching stylus at the points that a coating fails are called the critical loads of failure.

Case Study #6

Nanoparticle-based drug delivery systems have become increasingly popular over the last 20 years. Whether these systems are stabilized electrostatically or sterically (using proteins, polymers, or targeting vectors) the dispersion must be stable at physiological pH and salt concentrations. Zeta potential has become the standard tool to assess the pH-dependent stability of nanoparticle dispersions.

Zeta potential is not measurable directly but it can be calculated using theoretical models and an experimentally-determined electrophoretic mobility. When an electric field is applied to charged particles in the colloids, particles move toward an electrode opposite to their surface charge. Electrophoretic light scattering is the method most popularly used to determine the velocity of the particles suspended in a liquid medium under an applied electric field.

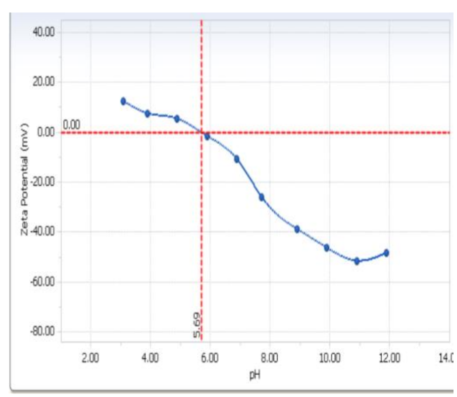

Figure 6. Zeta potential analysis of a particulate dispersion.

Litigation and IP Support

Ebatco can provide expert testimony and data analysis to help with the patent process as well as any infringement issues. Previously, we have assisted clients by providing patent claims support to help protect their intellectual property.

Case Study #7

A material is considered hydrophilic, or water attracting, if the contact angle made by water on the substrate is less than 90°. This means that the water will wet the surface of the material and interact with the surface molecules. Hydrophobicity is a phenomenon that is observed when water is deposited on a substrate and the contact angle is 90° or higher. This means that water will be less likely to wet the surface or interact with the surface.

Water is used as the depositing liquid to test the contact angle with the surfaces, which will determine the wettability of each surface. To illustrate the degree of wettability on a desired substrate, water contact angles on both stainless steel and PTFE were investigated (Figure 7). It can be noted that surfaces with higher contact angles are less likely to have particles adhere to the surface and would be ideal when used in water-resistant applications.

At ambient laboratory temperature and humidity the contact angle of water on stainless steel is 74.1°, and the contact angle of water with PTFE is 109.3°. Due to this result, a correlation can be made that the water has a higher degree of wetting on the stainless steel substrate compared to that of PTFE. From a wetting and adhesion point of view, PTFE would be a better non-stick substrate than stainless steel.

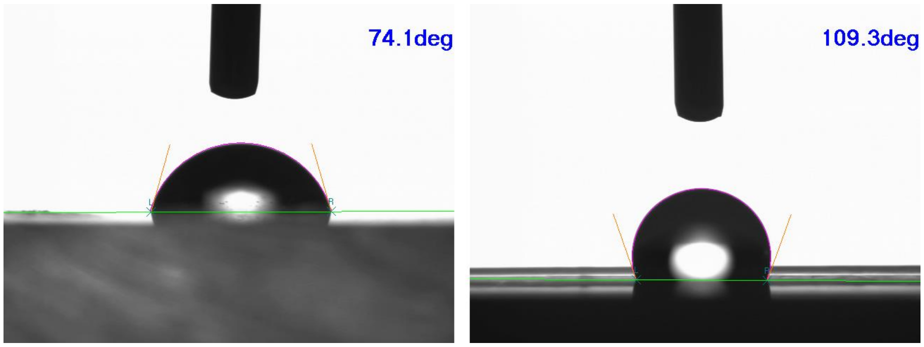

Figure 7. Water contact angle measurements on steel (left) and PTFE (right).