



Brooks Instrument

Applying Thin Film Coatings Used in Medical Devices | Business White Paper

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Applying Thin Film Coatings Used in Medical Devices

Society has benefited tremendously from the development and utilization of mechanical devices which are implanted inside the body and are used to replace bones and joints, increase blood flow, and even measure blood chemistry. To further enhance the performance of these devices, the application of thin films to the external surfaces is an ongoing research and development interest at many companies. Engineers have a choice of a variety of technologies to apply these liquid coatings to these often complex surfaces ranging from vacuum technology to direct liquid application. The decision on what technology to use is a function of the liquid precursor used, the mechanism of coating formation and the geometry of the object to be coated. A critical quality and process control criterion is the consistency of the coating on the surface. Fluid delivery technology can play an important part in maintaining coating consistency. Pumps and liquid flow controllers are technologies being used today. For vapor coating processes, liquid vaporization technology is a critical link in the fluid delivery system. New flow and vaporization technology is available that can be applied to fluid delivery to improve the application of medical device coatings.

Why Coating

The human body has defense mechanisms that normally treat foreign objects as a threat. This is great when the foreign body is a bacteria or a virus, but in relation to medical devices, this response can affect their performance. Certain metals and plastics have surface properties that make them somewhat compatible in the body. In many applications, these materials don't have the proper physical properties to make them useful for a specific function. Other materials might be better from a mechanical standpoint, but are more irritating to the body. Coatings are also used to extend the useful life of the device in the body. Here are just some of the uses of medical coatings.

- To reduce friction of the medical device in the body to improve the placement of the device and also minimize irritation and inflammation
- To reduce the formation of scar tissue surrounding implanted devices
- To encourage the growth of tissues to help the healing process
- To reduce the chance of infection related to the implanted device
- To "hide" the device from the body's self defense mechanism
- To measure body chemistry in real time

The coatings applied to the surface can be as simple as a thin metal coating or as complex as polymer coating interlaced with precise pores that time-release drugs.

Coating Challenges and Solutions

Applying a coating to a device that is placed in the body is a very critical process. The potential detrimental affects of the coating must be thoroughly investigated prior to official approval for market introduction. Here are some of the many challenges facing an engineer when designing techniques for coating medical device structures.

- Complex substrate geometry
- Even coating over the complete surface
- Consistent thickness and mass of coating across a production lot
- Eliminating bridging across web structures
- Coating adhesion and eliminating post implant particle generation
- Applying high molecular weight active drug molecules
- Creating porous films that allow time release of drugs

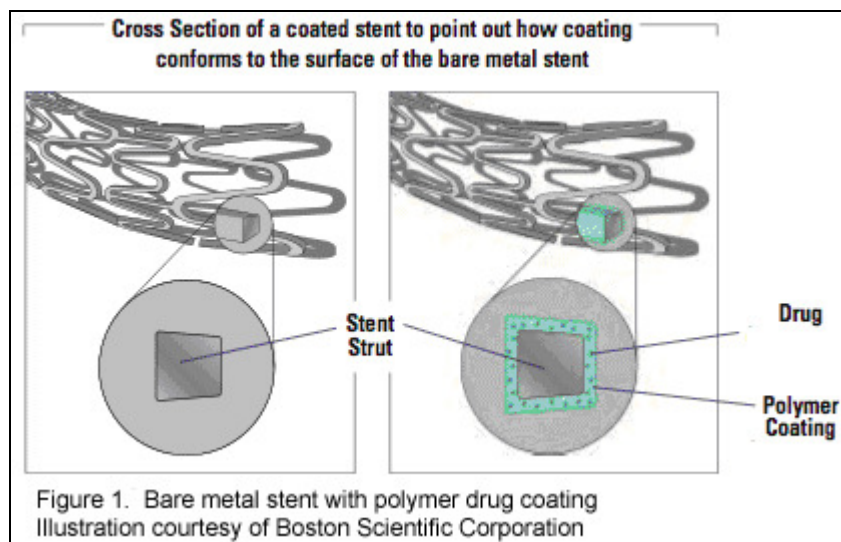
To create the coating, an engineer has a choice of a variety of technologies. These include:

- Dipping the object in a liquid and removal to create a thin surface film
- Spray coating to deposit a thin film
- Physical vapor deposition to transfer a solid source to a surface film
- Chemical vapor deposition for a surface reactions to create film
- Freeze condensation of vapor to create a thin film of frozen liquid
- Surface condensation to create a film of liquid
- Surface polymerization to create a film from a monomer vapor
- Ink jet placement of coating via impingement of tiny droplets

In each of these technologies, coating thickness and uniformity are functions of the rate of delivery of liquid or the vapor concentration at the surface of the part.

Example of a Coated Medical Device - Drug Coated Cardiac Stents

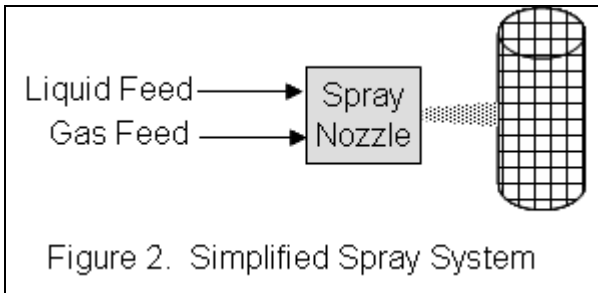
A porous polymer matrix containing time release drugs is now being used to coat bare metal stents to inhibit restenosis. The implantation of stents using balloon angioplasty is an acceptable treatment for opening a constricted or partially blocked artery. An intricately laser cut metal stent is placed in the blockage and expanded to open the artery. The expanded stent keeps the artery open. However, in approximately 25% of patients, restenosis will occur, which is scar tissue build-up around the stent that can cause a re-blockage. Drugs have been developed that inhibit scar tissue cell formation and are fixed in a polymer matrix for time release to the surrounding tissue. The coating has to be pliable to withstand stretching as the stent is expanded and must also have high adhesion to the stent's surface to prevent the coating from breaking off the surface and into the bloodstream. The final coating surface has to be smooth and continuous over all areas. Figure 1 illustrates the complex shape of the stent and the polymer drug coating on the surface of the stent.



Spray Coating Technology

Simple dip coating has not been successfully used for stent coating because polymeric bridges can be formed between web elements. Spray coating, as illustrated in Figure 2, is a technology that has been successfully used for depositing a polymer film on stents. Ultrasonic spray nozzles

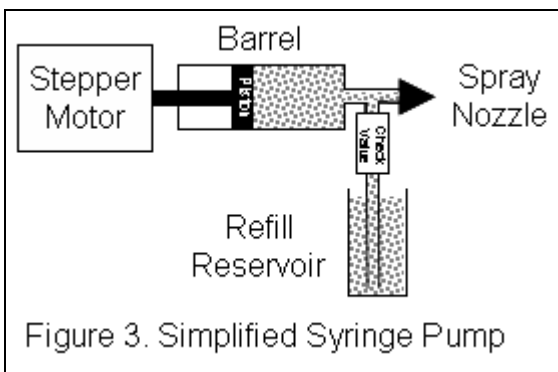
are used for creating the correct droplet size that when impacting the surface will adhere and dry at the proper rate to create a smooth finished film. A low flow of gas carries the ultrasonic created droplets to the surface of the stent in a narrow pattern. The sprayed liquid consists of a polymer/drug system dissolved in a suitable solvent to a concentration of 0.5 to 2% by weight.



Pump Liquid Delivery Control

Control of spray density to the stent surface is determined by the accuracy and consistency of the liquid and gas feed rate to the spray nozzle. Spray density will determine the coating thickness on the surface. A common liquid flow control solution is the use of a syringe pump as illustrated in Figure 3. A syringe pump is a positive displacement liquid flow control technology that uses a digital stepper motor to incrementally move a piston in a barrel in small discrete movements. A control circuit maintains the speed of the piston in the barrel to deliver fluid at a specific rate. The quantity of liquid dispensed per step is determined by the travel distance per step and the cross sectional area of the barrel. To increase low flow resolution, the diameter of the barrel can be decreased. The problem this introduces in production environments is at the end of the piston stroke, the barrel has to be refilled by withdrawing the piston slowly and pulling liquid from an external reservoir. A common problem when refilling the barrel is the formation of a gas bubble as the pressure of the liquid is reduced. The gas bubble has to be removed to keep the liquid incompressible for good flow control.

The step-like movement of the piston in the barrel will result in pressure fluctuations in liquid flow to the spray nozzle. These fluctuations result in short term unsteady spray density which can result in uneven part coating coverage.



Precision Spray Technology

In continuous production environments an alternative liquid delivery control technology is desired. Precision spray control systems utilize active control devices for liquid and gas flow. The spray density is directly proportional to the liquid mass flow rate to the spray nozzle as illustrated in Figure 4. The benefit of such a system is the spray mass delivery rate to the part can be precisely controlled. Flow can also be started and stopped quickly to minimize the consumption of expensive materials. The key elements of a precision spray control system can be visualized as a chain, with reliability dependent on the strength of the weakest link. The key elements of the supply chain consist of the liquid and gas supply system, the liquid and gas flow controller technology and the spray nozzle technology. A gas pressurized liquid in a container supplies the fluid to the system. The size of the container can be sized for a typical lot to improve productivity of the process.

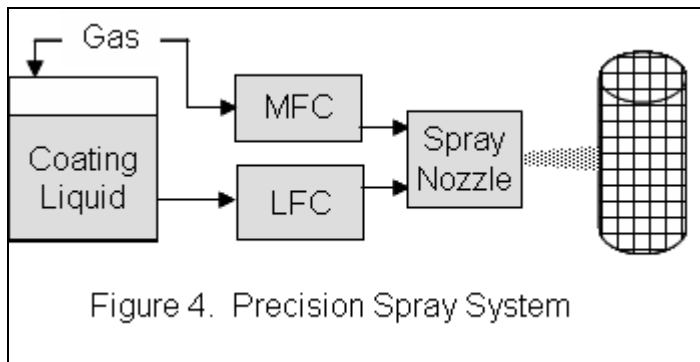
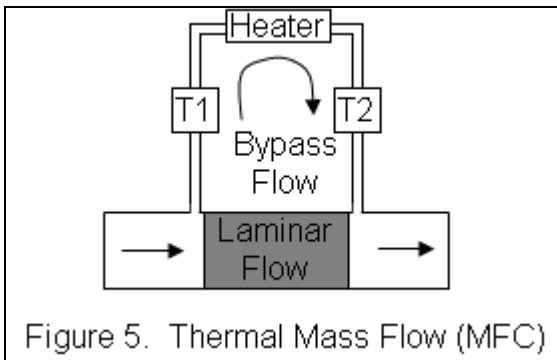


Figure 4. Precision Spray System

Gas and Liquid Flow Control

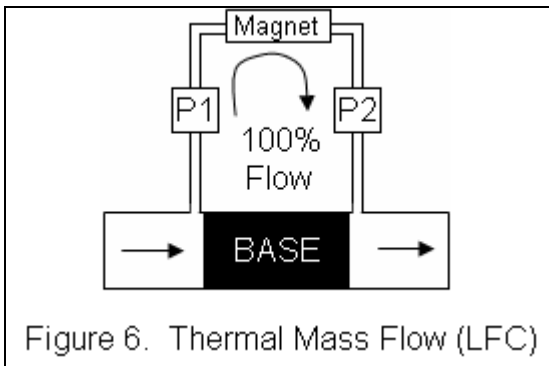
One of the key attributes of a precision spray system is the active control of liquid and gas feed rates to the spray nozzle. A simple pressure regulator is not sufficient to control the flow of gas to the spray nozzle. This active control allows the process engineer to precisely set the mass feed rate of the precursor to the nozzle. The accuracy and precision of the liquid and gas feed controllers will reduce the part-to-part variability of film deposition rate.

Carrier gas flow control is accomplished using a thermal sensor mass flow controller (MFC) as illustrated in Figure 5. This device uses the heat capacity of a pure gas to infer the mass flow rate of gas to the vaporizer. The equation to be solved is a simple one: $\text{mass flow} = (\text{heat added to the gas}) / ((T_2 - T_1) \times (\text{heat capacity of the gas}))$. A laminar flow element is used to create a linear relationship between pressure drop and flow. The created pressure drop forces a very small portion of the gas to pass through the sensor tube in proportion to the overall flow. An integrated control valve, along with digital electronics completes the gas mass flow controller.



In the last few years a new mass flow technology, based on Coriolis principles, has been utilized for liquid mass flow control in precision spray systems. Coriolis mass flow measurement technology has been historically used in many industries where accurate, reliable measurement of liquid mass is a requirement. Advances in sensor design and electronics processing have allowed Coriolis sensors to be reduced in size in order to measure the low flows found in medical device coating.

A Coriolis sensor utilizes a vibrating tube to measure the mass flow of liquid. The momentum of the moving fluid changes the shape of the vibrating tube. A U shaped tube is a typical sensor design for these low flow sensors as illustrated in Figure 6. Every Coriolis mass meter has 3 key components: the sensor tube which is mounted rigidly on a base, position sensors which measure the inlet and outlet legs of the tube, and a magnetic drive which vibrates the tube. All of the flow goes through the sensor tube, and so there is no bypass as in the thermal mass flow device.



In a no-flow condition, the inlet and outlet legs of the tube vibrate in unison and the result is a differential electrical signal from the two position sensors of zero time. In a flowing condition, the inlet and outlet legs of the tube vibrate out of phase and the result is a differential electrical signal from the two sensors with a specific time lag. When the sensor is factory calibrated using an inert fluid, the amount of time lag created by the moving fluid is directly proportional and linear to the fluid mass flow. Thus, a Coriolis sensor is a universal mass flow measurement device with measurement accuracy independent of the physical and thermal properties of the fluid. This makes Coriolis sensing technology ideally suited for accurate measurement and control of fluids with unknown properties such as advanced multi-component coating fluids. Coriolis sensors are also very fast in responding to changes in flow.

The natural resonant frequency of a Coriolis sensor can be used to determine fluid density. A heavy fluid in the tube will reduce the natural frequency while a light fluid or gas will increase the natural frequency. Fluid density measurement is very useful to determine when a solvent has flushed out the coating fluid from the system.

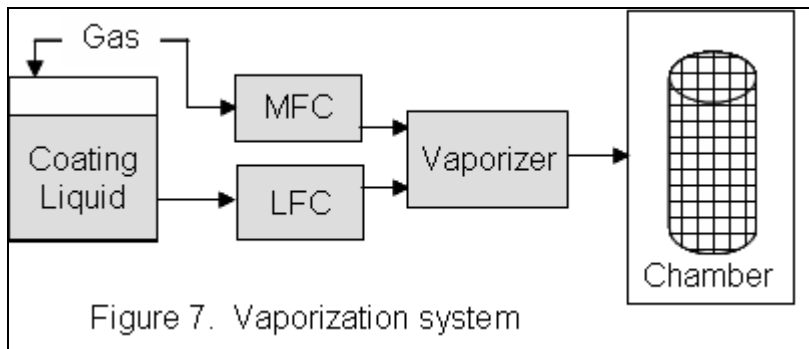
Quality and Production Control Benefits

The benefit of a closed loop control precision liquid coating system is the presence of flow measurement devices. These devices not only maintain flows to an exact setpoint but also generate data that can be used by quality control personnel to be able to minimize variability in the process. Software alarms warn if the fluid flow rates cannot be maintained and allow the process to be modified before out of spec product is produced.

Liquid Vaporization Coating Technology

In some applications the required coating is so thin or the material must be reacted on the surface to create a film that spray coating technologies are inadequate. An alternate technology for coating is to convert the liquid flow to a vapor and then immerse the part in the vapor where a thin film is formed on the surface. This is illustrated in Figure 7. The mechanisms for vapor film formation include:

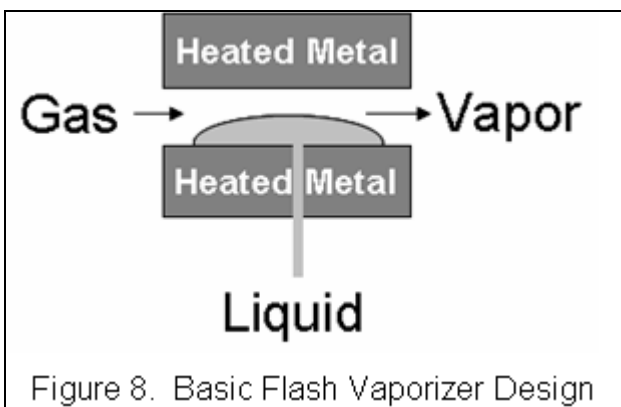
- Surface reactions
- Surface polymerization
- Surface condensation
- Surface freezing



Flash Vaporizer

Conventional vaporizers, also called flash vaporizers as illustrated in Figure 8, rely on direct liquid contact with a heated metal to transmit the energy required for vaporization. A carrier gas is used to dilute the vapor, which reduces its dew point and also transports the vapor to the chamber.

Three factors can influence the rate of heat transfer to a liquid during this heating step: the temperature difference between the liquid and the metal heating surface, the area of the metal/liquid surface to transfer the heat, and the overall heat transfer coefficient for the system. This is summarized in the following simple equation: $m \Delta H = kAdT$ where k is the heat transfer coefficient of the system (function of the properties of the liquid, gas and metal, usually is a constant), A is the area available for heat transfer, dT is the temperature difference between the liquid and the heating surface, m is the mass flow of precursor and ΔH is the enthalpy of vaporization



A flash vaporizer relies on a small surface area to transmit the heat to the liquid. The net result is the temperature of the metal must be high enough to transfer heat to the liquid in a short time period. Vaporizers typically operate at pressures near the chamber pressure. A phenomenon can occur during flash vaporization at the heated surface in contact with the liquid, where vapor is generated at this interface and, as it expands, can lift the liquid off the surface. The vapor then acts as an insulator and stops the heat transfer to the liquid which, after cooling, contacts the surface again.

This is similar to the dancing of a droplet of water on a hot cooking surface. When this happens in a vaporizer, the vapor production is not at a steady state. Fogging can be a result of this unsteady behavior at the outlet of the vaporizer. Contact of the liquid with the high temperature metal can also result in thermal decomposition which can eventually plug the vaporizer and create particles.

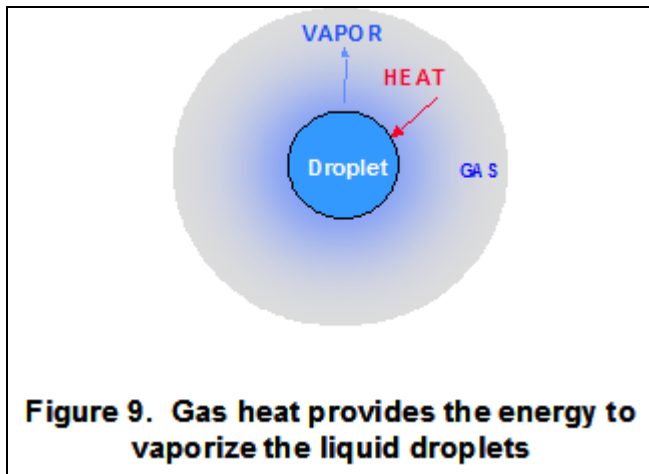
Low Temperature Vaporization

Many liquids that must be vaporized for film formation have very low vapor pressures and are also sensitive to thermal decomposition. A vaporizer design for thermally sensitive precursors would create a very large surface area (in the form of droplets as illustrated in Figure 9) to transmit heat to the liquid. Increasing the effective vaporization surface by a factor of a thousand results in a greatly reduced differential temperature required to drive heat into the liquid. The electrical heater should also have a very large area to reduce the heat flux or surface temperature of the heater. Liquid to metal contact is avoided by using the carrier gas to conduct energy from the electric heater to the liquid surface.

A phenomenon called wet bulb depression will occur that helps to reduce the liquid temperature during vaporization. The term “wet bulb temperature” comes from meteorology and is the lowest temperature that can be obtained when evaporating water into air. Wet bulb depression is the difference between the water temperature during evaporation and the actual air temperature. The same terminology can be applied to evaporating high boiling liquids into a dry gas.

The temperature of these liquids in contact with a hot gas will be substantially lower than the gas temperature. Decomposition reactions occur much faster in a liquid than a vapor. Keeping the liquid cool during the vaporization step will reduce decomposition and solid formation.

Increasing the surface area also reduces the time required to vaporizer liquid. The calculated vaporization time for liquids with high surface area is very short.



The final result of such a design is a gentle vaporization of liquids used to create films in medical devices. Low temperature vaporizers are now being employed to create films used in the production of implantable blood chemistry sensors.

Conclusion

The development of new coatings to enhance the performance of medical devices will continue to be an area of intense research interest. New flow control technologies have been developed that improve the production process, especially in the area of liquid spray coating technology. Improved coating uniformity and part-to-part repeatability are benefits of using this technology. If direct liquid coating cannot be applied, new vaporization technology is available which can generate controlled vapor flow for precision coating applications.

About the Author

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Wesley Sund has a BS in Chemical Engineering. He has over 30 years experience in chemical processing and process instrumentation. Recently he has been working with the medical device industry to develop advanced coating solutions for medical devices.