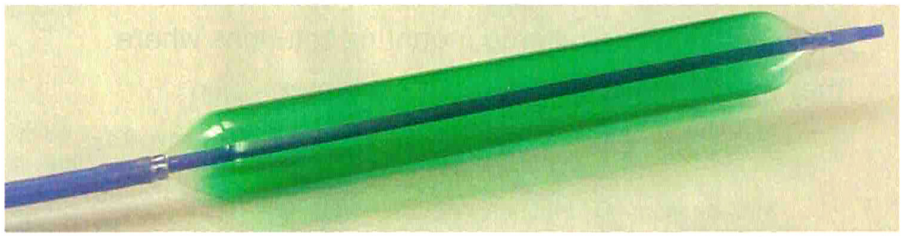
# Texturing Prospective with Ultrasonically Coated Balloon Catheters

Drug-coated balloons may soon enter the evolutionary path for clogged artery therapies that has gone from bypass surgery to angioplasty balloons to stents. As such, manufacturers should explore the best processes and practices for this up and coming device. This article looks at the impact of textured drug coatings and balloons using ultrasonic spray technology for this emerging treatment modality.

*By Fielding Water, Applications Engineer, Sono-Tek Corp.*



Drug-coated balloons (DCB) emerged at the crossroads of angioplasty balloons and drug-eluting stents in treating blood vessel obstructions. Intense research continues as medical device manufacturers compete to create better products and processes. While the first generation of DCBs has been released in Europe and clinical data is being collected, DCBs are predicted for launch in the United States by mid-2015 upon FDA approval.

Balloons for angioplasty, or the mechanical widening of obstructed arteries, succeeded the drastically more invasive bypass surgery. It became the regular procedure for treating semi-clogged arteries; however, it is often not a long-term solution as arteries can become clogged again or the vessel walls can become weakened due to over-inflation.

To avoid acute relapse, stents were developed to maintain the reopening of an artery for extended periods of time. Although stents performed this function well, they caused immune responses that trigger increased scar tissue growth and reclogging of the vessel.

In 2003, the first drug-eluting stent was approved by the FDA. The use of antiproliferative drugs prevented the buildup of scar tissue in the arteries. However, the drugs can cause blood clots or hypersensitivity, and patients who have drug-eluting stents commonly take blood thinning medication.

What developed from the difficulties of uncoated balloon angioplasty and drug-eluting stents is drug-coated balloons. The balloon is inserted via catheter, directed to the lesion, and inflated for 30 seconds up to a minute. The drug on the balloon is released during this time, and attaches to the blood vessel lining. Over the next few days, the medication is gradually absorbed by the vessel walls into the tissue. This results in long-lasting effects of the drug, even with a short release period.

## Texturing Within the Drug Coating

Gauging an object by the consistency of its surface is determining its texture. Textures can range from amorphous to crystalline, or smooth to rough. This range can be achieved for different balloons coated with exactly the same amount of drug. What causes these differences in coating is cohesion. Cohesion is the strength of the bonds between the various molecules in the coating. Depending on the method of drug application, the molecules experience varied cohesive forces when applied to the balloon. This leads to different drug molecule interactions, and ultimately, different coating textures (Figure 1).

By reducing the surface area of the coating, less of the bulk coating is exposed. Lower exposure reduces compromise of coating integrity during storage or transit through a blood vessel. Amorphous coatings limit drug loss. By the same token, reducing the surface area also reduces drug delivery upon inflation at the lesion site. On the other hand, increasing the surface area of the coating promotes drug delivery upon balloon inflation. A rougher coating results in greater contact of the coating with the vessel wall, encouraging absorption. However, this coating texture also increases drug transit loss before the balloon reaches the target location, and coating integrity can also be more easily compromised during storage. Fine tuning of

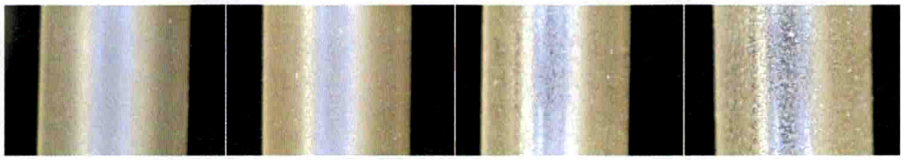


**Figure 1: Four separate balloons with identical drug deposition densities**

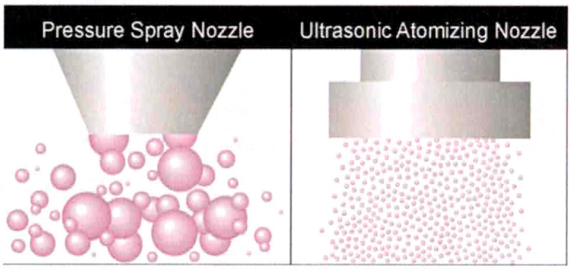



**Figure 2: Comparison of droplet size distribution between pressure and ultrasonic nozzles**

the drug coat texture is necessary to meet the requirements of individual company approaches to drug-coated balloons. Ultrasonic spray provides that versatility to take advantage of what texturing has to offer.

Ultrasonic spray coating provides great process flexibility and reliability in creating and reproducing a range of textures. Unlike conventional spray techniques, ultrasonic nozzles do not rely on pressure to shear the solution into droplets. The lack of pressure greatly reduces raw material use and waste generation. Using high frequency vibration, mathematically defined capillary waves on the nozzle tip create drops within a very narrow drop size distribution – only microns large. Using air shaping, the droplets are guided to the balloon to create a coating of the drug solution. It is the fact that ultrasonic spray creates a homogenous output that must travel a distance to the balloon that allows it to successfully create a range of coating textures (Figure 2).

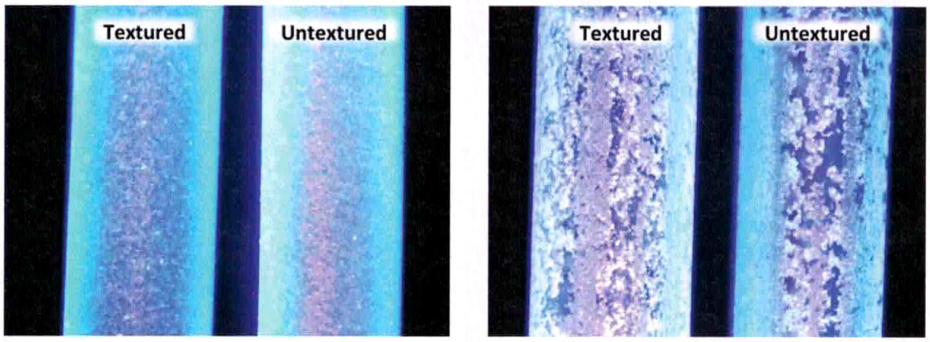



**Figure 3: Identically coated textured and untextured balloons (left). Balloon coatings after undergoing stress test (right)**

## Texturing of the Balloon

While clinical data is being collected for the currently available DCBs, companies are working to create the next generation of balloons, improving drug-polymer bond quality and methods to reduce manufacturing cost. One development path involves mechanically texturing the balloon surface prior to drug coating as a primer to improve the coating adhesion. One critical element to modifying the surface of any balloon is to attain the textured surface without altering the performance characteristics of the balloon.

Similar to altering the morphology of the drug coating, texturing the balloon increases the contact surface area for the drug coating. This allows for greater adhesion, or strength of bond between the drug coating and the balloon. A durable coating will develop when the drug solution comes in contact with the balloon and adheres before drying. Bond formation and adhesion begin with interfacial molecular contact by wetting. Increasing the surface area directly increases contact and bond formation of the coating to the balloon. The greater adhesion helps prevent the drug coating from prematurely separating from the balloon, potentially allowing for less drug loss or damage during post processing of balloons within the manufacturing process. Texturing helps protect the integrity of the balloon coating during the manufacturing process and during transit of the balloon to the target site inside the body.

To investigate coating adhesion, two samples of balloons were identically coated and put to the same stress test. The textured and untextured balloons had identical single wall thickness and performance specifications. Prior to coating, a small amount of ultraviolet dye was added to a drug solution. When viewed under ultraviolet light, the dye provided a vibrant contrast, making inspection of the integrity of the coating possible. After performing blood vessel transit simulation, the samples were illuminated under a black light to inspect the resulting coating integrity. Great care was taken to apply stress to the balloons in a reliably repeatable fashion. Figure 3 illustrates the adhesion quality of the coatings.

The drug coatings prior to the stress test appear very similar. The quality of the drug adhesion to the balloon does not impact the bulk characteristics for the performance of the coating. Texturing the balloon affects the interface between the balloon and the coating, not the coating itself.

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In comparing the drug coating after the stress test, an observable difference in the integrity of the coating was seen. In general, more of the drug coating was lost from the untextured balloons (dark blue spaces), while the textured balloons retained more of the drug-polymer coating. This supports the concept that textured balloons increase coating adhesion. By bonding better to the balloon, less of the drug was removed when stress was applied. As a result, greater contact of the drug with the balloon surface was achieved with less risk of coating fragmentation of the coating, during both the manufacturing process and the clinical application of the product.

## Conclusion

For medical device manufacturers, effectively developing drug-coated balloons to clear clogged arteries requires capable equipment for research and production. For companies to fully exploit the advantages texturing can offer, a coating process with the capability to create variable textures is a necessity. As research and innovation shape the future of drug-coated balloons, so must the manufacturing capability keep pace. With its high reproducibility and tremendous process flexibility, ultrasonic spray technology coupled with textured balloons can both direct ongoing research and keep abreast advances in drug-coated balloon technology. MDT

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