

MEDICAL DEVICE & DIAGNOSTIC INDUSTRY

Radiopaque Polymer Formulations for Medical Devices

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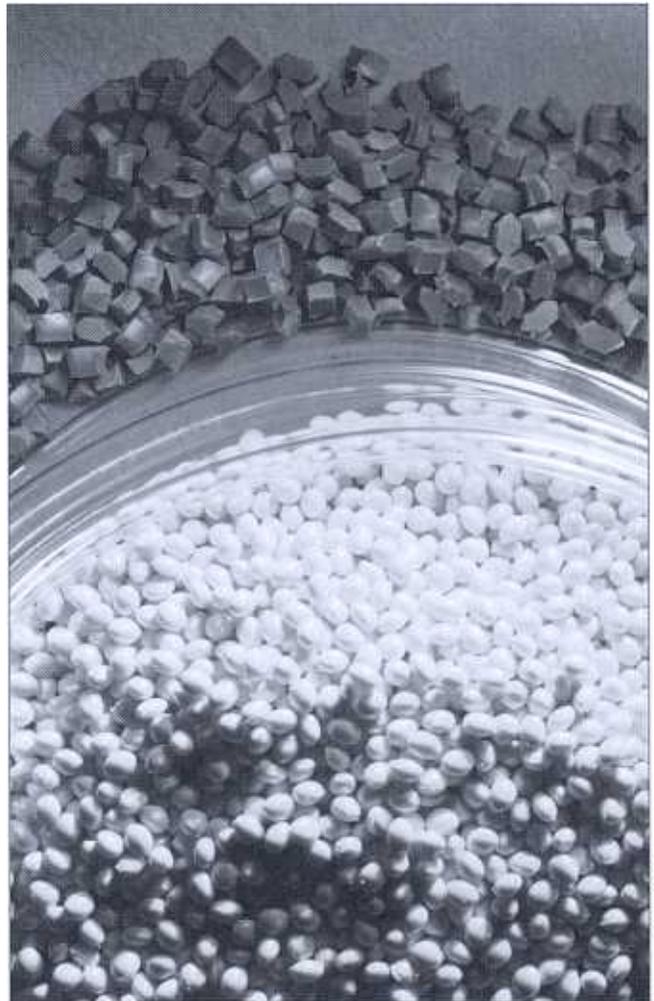
Custom blending of radiopaque fillers can increase the opacity of catheters and other devices, making them clearly visible under fluoroscopy and x-rays without sacrificing the mechanical properties of the polymers.

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POLYMERS used to produce catheters and other devices that are inserted into the body for diagnostic or interventional procedures are commonly filled with substances opaque to x-rays, thereby rendering the devices visible under fluoroscopy or x-ray imaging. These fillers, or radiopacifiers—typically dense metal powders—affect the energy attenuation of photons in an x-ray beam as it passes through matter, reducing the intensity of the photons by absorbing or deflecting them. Because these materials exhibit a higher attenuation coefficient than soft tissue or bone, they appear lighter on a fluoroscope or x-ray film. This visibility provides the contrast needed to accurately position the device in the affected area. Image contrast and sharpness can be varied by the type and amount of radiopacifier used, and can be tailored to the specific application of the device.

For example, a device designed for use near the surface of the skin requires less radiopaque filler to achieve the required level of attenuation compared with one used inside the coronary vasculature. Device design is also a factor: a higher loading of radiopaque material, for instance, is needed for thin-wall catheter tubing than for products with thicker walls. Generally, compounds should contain only the amount of additives absolutely required for the application, since overloading can result in the loss of the polymer's mechanical properties. Blending together several radiopaque materials can produce better results than using only one type in a formulation.

Among the most widely used radiopacifiers for medical devices are barium sulfate, bismuth compounds, and tungsten—metals that are excellent absorbers of x-rays. Selection of the correct fillers in the proper amount requires a thorough understanding of attenuation and how it is affected by various radiopaque compounds. This article discusses those radiopaque





fillers commonly used with medical-grade thermoplastic polymers and the factors involved in their selection.

UNDERSTANDING X-RAYS

X-rays are a form of radiation, part of the electromagnetic spectrum consisting of energy waves of widely differing frequency and length. Produced by the oscillation or acceleration of an electric charge within a magnetic field, these waves range from those with very high frequencies and short wavelengths to those with very low frequencies and long wavelengths (Table I).

Diagnostic x-rays fall near the shorter-wavelength end of the spectrum, measuring between 1 Å—about 4 billionths of an inch long—and 0.1 Å. X-rays are produced from the conversion of energy that results when fast-moving electrons from the filament of an x-ray tube interact with a tungsten anode or target. The kinetic energy of the electrons increases as voltage, expressed as peak kilovoltage (kVp), is increased. The intensity of an x-ray beam is determined by the number of photons in the beam and the energy of the photons, which is expressed as kiloelectronvolts (keV).

Shorter-wavelength x-rays exhibit greater energy and penetrating power than do longer ones (Table II). For example, 0.1 Å is equivalent to about 124 keV of energy, while 1.24 Å equals only 10 keV. A voltage of 100 kVp—the standard rating of older-model x-ray machines—will not have all photons at 100 keV. Typically, 100 kVp produces < 1% of photons at a 0.1-Å wavelength, whereas the other 99% are longer and have less energy. Photons with ≥15 keV can ionize atoms—causing the loss of an electron—to produce ionizing radiation. Gamma rays, x-rays, and some UV rays are considered ionizing radiation.

Energy attenuation relates both to the quantity and the quality of the photons in a beam. Increasing the energy increases the

number of photons transmitted and generally decreases the degree of attenuation. The precise nature of the radiation affects attenuation, as does the density, atomic number, and electrons per gram of the absorbing or radiopaque material. An increase in any of these factors decreases the number of transmitted photons and thus increases attenuation.

In an x-ray beam, both the transmitted and attenuated photons are important in producing an accurate image. Different types of tissues attenuate energy differently, which provides contrast in the x-ray image. A dense element such as barium, with an atomic number of 56, has a higher attenuation coefficient and

X-ray transmission generally increases and attenuation decreases when radiation energy is increased.

absorbs x-rays better than matter that is less dense. The higher the attenuation coefficient, the lower the number of transmitted photons. Density, which is directly proportional to attenuation, determines the number of electrons that are present in a given thickness of material and, thus, the photon-stopping power. Denser materials appear as lighter images on an x-ray film or a fluoroscope, which displays a moving image when a beam of penetrating radiation is transmitted through the body onto a viewing screen.

Differences between attenuation of bone and soft tissue under low-energy radiation are produced by differences in the number of photoelectric reactions, which involve the formation and liberation of electrons during electromagnetic radiation. The calcium in bone has a higher atomic number than that of the surrounding tissue, causing more reactions and increased attenuation. At higher energy levels, however, variations in attenuation depend more on interactions known as Compton scatterings, which are changes in wavelength that occur when the waves are scattered.

As mentioned, x-ray transmission generally increases and attenuation decreases when the radiation energy of a beam is increased. But this does not hold true with high-atomic-energy absorbers such as, for example, iodine (atomic number 53). Transmission may decrease with increased beam energy because of the likelihood of a photoelectric reaction occurring as the energy approaches the binding energy of an inner-shell electron. A photon needs a minimal amount of energy—more than the binding energy of the electron—in order to eject an electron. High-energy photons are thus less likely to be transmitted than low-energy photons.

For some elements, an important property for diagnostic radiology is the K-shell binding energy, known as the K-edge (Table III). For example, an x-ray of 33 keV will not eject an electron from the K-shell of iodine, which has a K-edge of 33.2 keV. A photoelectric reaction has a greater chance of occurring when the photon energy and electron binding energy are nearly the same: that is, a 30-keV photon is more likely to react with the K-shell electron of iodine than is a 100-keV photon. Because

Type	Wavelength
Radio, television, radar	3×10^5 to 1 cm
Infrared radiation	0.01 to 0.00008 cm
Visible light	7500 to 3900 Å
Ultraviolet radiation	3900 to 20 Å
Soft x-ray	100 to 1 Å
Diagnostic x-ray	1 to 0.1 Å
Therapeutic x-ray	0.1 to 0.01 Å
Gamma rays	0.1 to 0.000001 Å

Table I. The electromagnetic spectrum (1 Å = 10⁻¹⁰ m).

Wavelength (Å)	Energy (keV)
0.0005	24,800
0.08	155
0.1	124
1.24	10

Table II. Correlation between wavelength and energy.

electrons that are tightly bound in their orbits are most likely to be involved in photoelectric reactions, the K-edge of the absorber should be near the energy of the x-ray beam to ensure maximum x-ray absorption.

Polychromatic radiation, which contains photons of varying energies, is more complex in terms of attenuation than is monochromatic radiation. Both the quantity and quality of photons in a polychromatic beam change as they pass through an absorber. The peak kilovoltage of a polychromatic beam determines the mean energy, which falls between $\frac{1}{3}$ and $\frac{1}{2}$ of the peak, so that a 100-kVp beam has a mean energy of about 40 kV. In the case of a 100-kVp x-ray machine, barium, with a K-edge of 37.4 keV, is an excellent absorber. When the mean energy increases significantly, tungsten, with a K-edge of 69.5, becomes a better choice as a radiopaque material.

COMMON RADIOPACIFIERS

Barium Sulfate. Barium sulfate (BaSO_4) was the first radiopaque material to be widely compounded in medical formulations and is the most common filler used with medical-grade polymers. (Patients are often asked to swallow a solution of barium sulfate before an examination of their digestive tract.) It is an inexpensive material, costing approximately \$2/lb; its white color can be changed with the addition of colorants.

With a specific gravity of 4.5, barium sulfate is generally used at loadings of 20 to 40% by weight. While a 20% barium sulfate compound is typical for general-purpose medical device applications, some practitioners prefer a higher degree of radiopacity than can be provided by that loading. With striped tubing, for example, a 40% compound is standard.

A loading of 20% barium sulfate by weight is equivalent to about 5.8% by volume; 40% by weight equals 14% by volume (Table IV). As the barium content moves beyond about 20% by volume, compounds begin to show losses of the base polymer's tensile strength and other mechanical properties. It is therefore best to formulate radiopacifiers at the minimum level for each application; excessive use of these fillers is not recommended.

Bismuth. Considerably more expensive than barium at \$20 to \$30/lb (depending on the chemical salt selected), bismuth compounds are also twice as dense. Bismuth trioxide (Bi_2O_3), which is yellow in color, has a specific gravity of 8.9; bismuth subcarbonate ($\text{Bi}_2\text{O}_2\text{CO}_3$) has a specific gravity of 8.0; and bismuth oxychloride (BiOCl) has a specific gravity of 7.7. Because of the density, a 40% bismuth compound contains only about half the volume ratio as a 40% barium sulfate compound. Since bismuth produces a brighter, sharper, higher-contrast image on an x-ray film or fluoroscope than does barium, it is commonly used whenever a high level of radiopacity is required.

Compared with barium, higher loadings are also possible: even a 60% bismuth compound can maintain the same base polymer mechanical properties as a 40% barium sulfate compound. A 20% bismuth loading by weight equals 3% by volume; a 40% loading by weight equals 7.6% by volume. Bismuth is sensitive to compounding and must be treated gently, with low-shear mixing recommended for optimum results. Because of their high levels of radiopacity, bismuth fillers have grown in popularity.

Tungsten. A fine metal powder with a specific gravity of

19.35, tungsten (W) is more than twice as dense as bismuth and can provide a high attenuation coefficient at a cost of approximately \$20/lb. A loading of 60% tungsten has approximately the same volume ratio as a 40% bismuth compound. Devices can be made highly radiopaque with relatively low loadings of tungsten, enabling good mechanical properties to be maintained. Because of its density, tungsten is typically selected as a filler for very-thin-walled devices.

A 50% tungsten loading by weight equals only 5.4% by volume; an 80% loading by weight represents 18.5% by volume. Tungsten is black in color, which cannot be changed with colorants. It is abrasive and can cause accelerated wear in extruders and other processing equipment. Devices filled with high loadings of tungsten will exhibit surface roughness. Because the material invites oxidation in the presence of oxygen and heat and is highly flammable, care should be taken while drying it. With elastomers, barium sulfate mixes better than do tungsten or bismuth compounds.

COMPOUNDING CONSIDERATIONS

Newer x-ray machines generally operate at higher energy levels than older ones—typically at 80 to 125 kVp as compared with 60 to 80 kVp for older machines. Higher energy radiation increases the transmission of photons and can require higher levels of radiopacity to provide the desired attenuation.

Element	Symbol	Atomic Number (Z)	K-Edge (keV)
Hydrogen	H	1	0.013
Carbon	C	6	0.28
Nitrogen	N	7	0.40
Oxygen	O	8	0.53
Sodium	Na	11	1.1
Aluminum	Al	13	1.6
Silicon	Si	14	1.8
Potassium	K	19	3.6
Calcium	Ca	20	4.0
Iron	Fe	26	7.1
Zinc	Zn	30	9.7
Selenium	Se	34	12.7
Yttrium	Y	39	17.0
Molybdenum	Mo	42	20.0
Silver	Ag	47	25.5
Cadmium	Cd	48	26.7
Iodine	I	53	33.2
Barium	Ba	56	37.4
Tungsten	W	74	69.5
Gold	Au	79	80.7
Lead	Pb	82	88.0
Bismuth	Bi	83	90.5

Table III. Atomic numbers and K-edges of elements used in diagnostic radiology.



Filler Type	BaSO ₄	Bi ₂ O ₃	W
Specific Gravity	4.5	8.9	19.35
% by Weight	% by Volume		
10	2.6	1.35	0.6
20	5.8	3.0	1.4
30	9.5	5.0	2.4
40	14.0	7.6	3.6
50	19.6	13.7	5.4
60	26.8	15.6	7.9
70	36.3	22.4	11.7
80	49.4	33.0	18.5
90	68.8	52.7	33.9

Table IV. Effect of density of filler on percentage by volume (BaSO₄ = barium sulfate, Bi₂O₃ = bismuth trioxide, W = tungsten).

Therefore, devices produced with barium sulfate compounds might not appear as bright on newer machines, for which bismuth compounds would be a better choice of radiopaque filler. Blending these materials, however, can often be the best solution, especially for multipurpose formulations used over a broad range of energy levels. A blend of barium, easily attenuated at low energy levels, and bismuth, attenuated at higher levels, often works well.

Compounding radiopaque materials is a complex business, involving many factors that can affect not only the degree of attenuation of the device but also the tensile strength, elongation, and other mechanical properties of the polymers. Care must be taken in selecting the right filler for the application, in the handling and drying of the materials, and in avoiding excessive shear heat during compounding so as not to degrade the polymer. Optimized filler loading will avoid either excessive or insufficient levels of the radiopaque material in the formulation. A

thorough knowledge of antioxidants, stabilizers, and colorants is also required when working with metallic fillers.

It has been said that compounding is similar to food preparation: given the same set of ingredients, a master chef will produce a better meal than a short-order cook. For many of the same reasons, products can vary in quality from one compounding house to another.

CONCLUSION

Medical devices used in diagnostic radiology must be easily seen on x-ray film and fluoroscopes in order for medical practitioners to precisely position them inside the body during critical procedures. The type and amount of radiopaque filler compounded with thermoplastic materials in the manufacture of these devices determines how they appear. The filler affects the degree of contrast and the sharpness of the image to the extent that it influences the attenuation of x-rays passing through the body and the device.

Successful material selection starts with an understanding of x-ray energy and attenuation. The effectiveness of the filler is related to the energy level of the x-ray equipment, the wall thickness of the device, the location inside the body where the device will be used, and the required mechanical properties of the polymer. The best compound for a specific application is often a blend of radiopaque fillers—such as a barium sulfate and bismuth compound—that provides the desired level of attenuation without the excessive loading that can degrade the polymer's mechanical properties.

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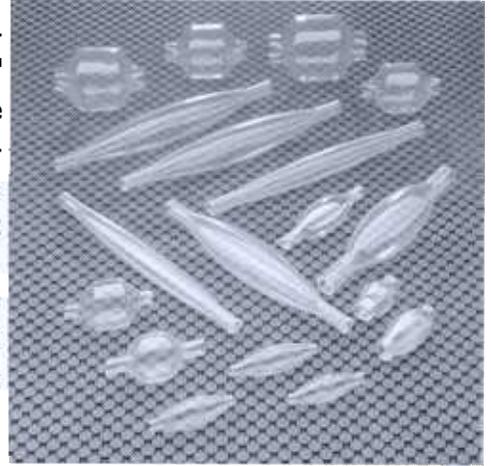
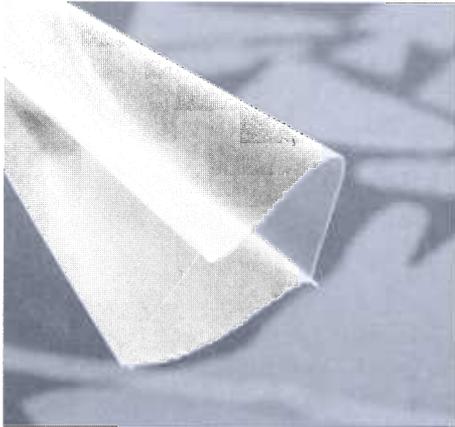
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