Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported being a member of the board of directors of the American Social Health Association; receiving payment from the American Social Health Association for developing educational materials on HPV prevention through an unrestricted grant to the association from Merck; recently completing a term as a member of Merck's Gardasil Male Population Advisory Committee; and receiving royalties from McGraw-Hill for his book, *Color Atlas and Synopsis of Sexually Transmitted Diseases,* 2nd and 3rd editions.

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In Reply: Dr Handsfield correctly points out that no data exist demonstrating that barrier protection prevents oral HPV infection during oral sex. Nevertheless, the Centers for Disease Control and Prevention encourages the use of barrier protection against sexually transmitted infections during oral sex and "with every sex act, from start to finish" in the hopes that this may prevent HPV transmission.[1]

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Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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RESEARCH LETTER

Changes to Polymer Surface of Drug-Eluting Stents During Balloon Expansion

To the Editor: Drug-eluting stents (DES) have advanced percutaneous treatment of coronary artery disease by reducing restenosis. However, DES have not eliminated restenosis, can serve as a nidus for thrombosis, and are associated with microvascular and endothelial dysfunction.[1,2] We hypothesized that the polymer surface of DES may be damaged during delivery balloon expansion and that microparticles may detach, which could contribute to these limitations.

Methods. We used optical microscopy to systematically image the polymer surface of the 4 US Food and Drug Administration–approved DES following expansion using the accompanying delivery balloon. The manufacturers (DES trade name in parentheses) are Abbott Laboratories (Xience V), Boston Scientific (Taxus Liberté), Cordis (Cypher), and Medtronic (Endeavor). They are deidentified as DES A, B, C, and D. A total of 5 stents were tested from each manufacturer in a vacuum filtration system containing a filtered test medium. Each stent came directly from its original package, premounted on its delivery balloon by the manufacturer, and not directly handled in any way. Although each stent was expanded unconstrained, the tests were otherwise conducted under a range of conditions that mimic regulatory submission requirements and the variability seen in clinical practice and to ensure that conclusions on the effect of manufacturer held averaging over a full range of deployment conditions. The 5 conditions (applied to 1 DES from each manufacturer) were delivery balloon maximum pressure of 9.0 atm, 14.0 atm, or 22.0 atm in deionized water at 25°C; and 14.0 atm in deionized water or plasma at 37°C. For control, a bare-metal stent was expanded using the same technique to a maximum inflation pressure of 14.0 atm in deionized water at room temperature.

Prior to expansion, the abluminal surface of each stent was imaged. Following expansion, all abluminal and adluminal surfaces were imaged. Additionally, all water and plasma solutions were filtered, and the filter and balloon surfaces imaged to identify any microparticles. The definitions of types of damage to polymer are: delamination, complete separation of polymer from stent surface; ridging, dislocation without detachment but with accumulation of polymer to form an elevated mass on the stent surface; webbing, distortion of the polymer such that material is stretched across and partially obstructs an open cell in between stent struts; peeling, partial but incomplete delamination of the polymer, which protrudes into the vessel lumen; and cracking, fine transection through entire polymer thickness.

Dispersive Raman spectroscopy was used for definitive identification of microparticles. Kruskal-Wallis tests were performed to determine if the proportion of the total surface area that was damaged differed by manufacturer. Analyses were performed using SAS version 9.2 and statistical significance was defined by a P value of less than .05 using 2-sided tests.

Results. Prior to balloon expansion, the abluminal polymer surface of DES D showed cracks; abluminal surfaces of all other DES appeared homogeneous. Following balloon expansion, the abluminal and adluminal polymer surfaces of all DES were damaged, affecting 4.6% to 100% of the surface area imaged (FIGURE and TABLE). In the Figure, the proportion of the surface area affected by each form of damage relative to the total surface area imaged was determined using quantitative image analysis. For webbing, the area of the 2 bases forming each individual web was used for the calculation.

No significant differences were observed between various expansion conditions for each particular DES; therefore results were pooled across conditions. Surface damage ranged from deformation (ridging, cracking, peeling, or webbing) to complete delamination with visually confirmed separation of polymer. The dimensions of damage and of detached microparticles ranged from 2 to 350 µm. Microparticles from all but DES B were confirmed to be polymer. The extent of damage differed by manufacturer ($P < .001$ for adluminal and $P = .002$ for abluminal damage).

Comment. In this preliminary study, balloon expansion damaged the polymer surface of DES and microparticles detached. The median proportion of total surface damage was associated with polymer type and involved both adluminal and abluminal surfaces.

Polymer damage during balloon expansion of DES has been reported by 2 research groups,[3,4] but is disputed by others.[5] Additionally, case reports of embolization of polymer

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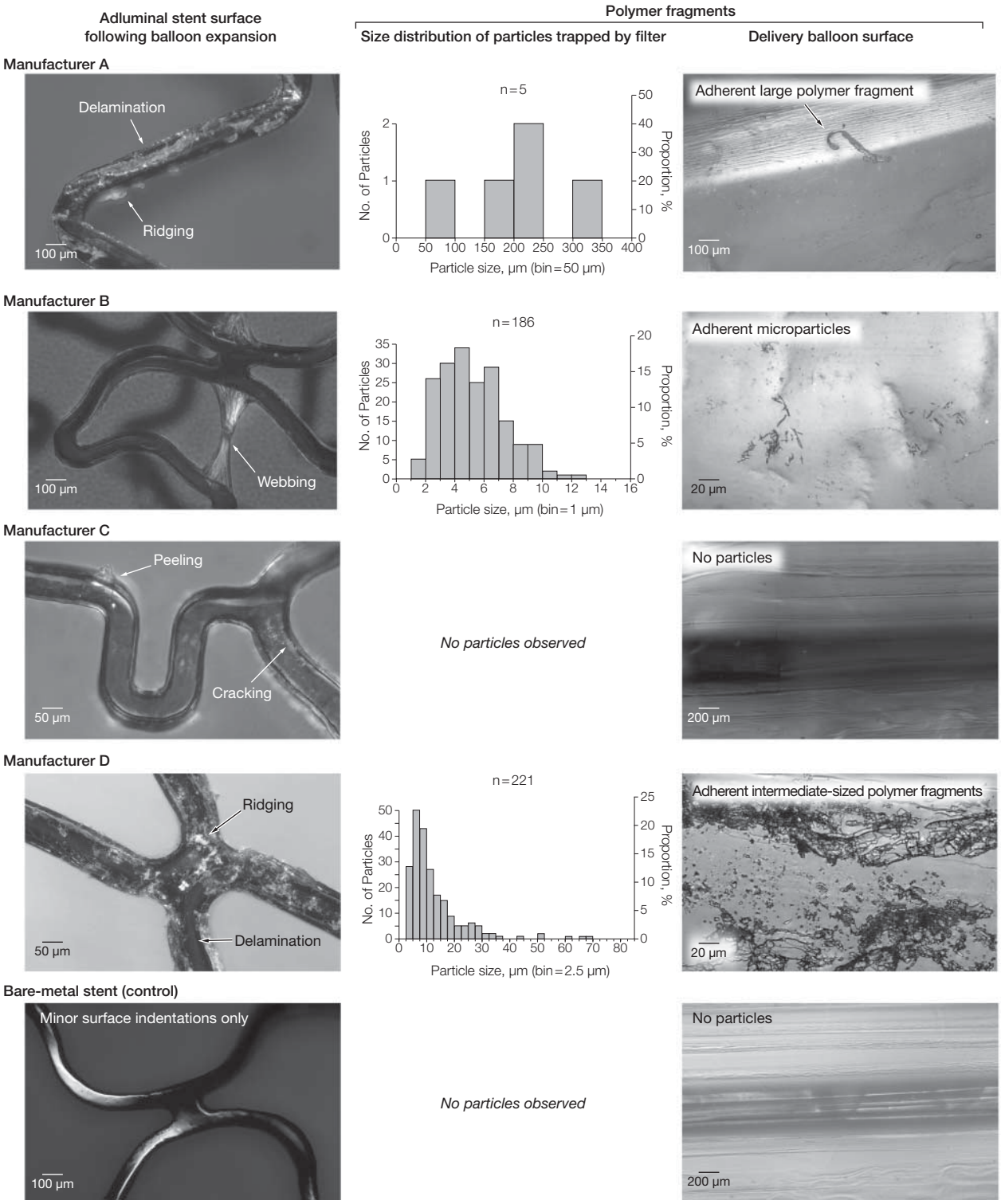
Figure. Representative Damage to the Polymers on the Adluminal Surface of Each Drug-Eluting Stent Following Balloon Expansion



Each stent shown was 3.0 mm in diameter and 16 to 18 mm in length. The adluminal and abluminal polymer surface of the drug-eluting stents were systematically imaged following balloon expansion using optical microscopy (Olympus BX 60; Olympus America Inc). Magnification was 50 to 500×. Each polymer surface was imaged at 16 locations (8 adluminal, 8 abluminal), spanning the length of the drug-eluting stents. The locations were predefined in a spiral configuration. For quantitative measurements, the magnification was 100×. Values in each bin interval are greater than the lower limit of the interval and less than or equal to the upper limit.

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Table. Proportion of Polymer Surface Damaged, Microparticles Shed, and Microparticles Adherent to Delivery Balloon[a]

Stent	Mean Proportion of Surface Damaged, % (95% CI)[b]		Microparticles[c]		Obstruction of Open Cells, Webbing
	Adluminal	Abluminal	Shed, Trapped by Filter	Adherent to Delivery Balloon	
A	41.7 (40.4-43.3); ridging, cracking, peeling, delamination	11.8 (9.2-14.5); cracking, ridging	Yes; (large size; smallest No.)	Yes; (small to large size; smallest No.)	No
B	14.7 (11.7-17.5); webbing, ridging	12.3 (10.1-14.6); webbing, ridging	Yes; (small size; intermediate No.)	Yes; (small size; intermediate No.)	Yes
C	4.6 (2.3-7.0); ridging, cracking, peeling	7.1 (5.2-9.0); ridging, cracking	None observed	None observed	No
D	100 (100-100); cracking, delamination, ridging, peeling	100 (100-100); cracking, ridging, peeling	Yes; (small to moderate size; largest No.)	Yes; (small to large size; largest No.)	No
BMS	0	0	None observed	None observed	No

Abbreviation: BMS, bare-metal stent.
[a] No significant difference existed between different conditions for each stent.
[b] Principal type of damage is listed in order of frequency.
[c] Parenthetical description is relative size (small, <10 μm; moderate, 10-100 μm; large, >100 μm [particles bordering on macroscopic]) and number (relative to other drug-eluting stents for which microparticles were shed or were adherent to delivery balloon).

fragments from other intravascular devices have been described and correlated with subsequent adverse clinical events.[6] However, there have been no published reports pertaining to DES.

Polymer damage and detached microparticles could theoretically contribute to DES-associated complications, including thrombosis, restenosis, and microvascular and endothelial dysfunction. Confirmation of our results would be useful, and further studies should determine physiological and clinical consequences of polymer damage and microparticle detachment. Additionally, the role of other components of DES (eg, drug and stent superstructure) require investigation. Data from this study may be used to calculate sample size for future biomaterial and engineering studies focusing on polymers and microparticles.

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Author Contributions: Dr Denardo had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Denardo, Carpinone, Batich.
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CORRECTION

Missing Letter Grouping Title: In the Letters section, a group of 2 letters to the editor and a reply letter published in the May 2, 2012, issue of *JAMA* (2012;307[17]:1797-1798) were missing a title. On page 1797, first column, after the letter by Pletcher and Kertesz, the title "Patient Requests for Nonbeneficial Care" should have preceded the letters by Cassel, Laws, and Brett and McCullough. This was corrected online.

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