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Introduction

Technologies and trends seeking to advance and change clinical practice

Advances in Cardiovascular Technology: State of the Industry and Emerging Markets, Vol. 4, is the fourth sourcebook concerning advanced cardiovascular technology produced by the staff of Medical Device Daily, part of AHC Media, a business of Thompson Publishing Group.

The sourcebook is not intended to provide an index of every company developing cardiovascular technologies. The intent of the book is to present the technologies under development that are most active in attempting to change the sector’s clinical dynamics, to highlight the primary technology trends in cardiovascular healthcare and to indicate the potential direction of these new developments.

Thus, we have selected companies on the basis of how well they represent these efforts. It is unlikely that all of these technologies and the companies pursuing them will reach fruition and turn into blockbuster opportunities (as drug-eluting stents did earlier in the decade). Some simply may not be payment-worthy — by either the reimburser or the private payer. And one or more may find themselves being superceded by a newer, more straightforward and cheaper technology. Another group may not have the management, resources or a workable enough business model to compete with others fighting for the same piece of the sector pie. But several are likely to significantly alter the landscape of cardiovascular therapy.

As such, this sourcebook offers a summary of companies that need to be watched over the long term, with lessons to be learned from either their successes or failures.

Technologies, issues and projections

As with the previous volumes, the emphasis of Vol. 4 continues to be on device systems rather than pharmaceuticals. Besides providing a description of these technologies, we attempt to provide a balanced perspective, each chapter describing these critical challenges as well as the significant opportunities.
The book is divided into three parts.

**Part I** provides a broad overview — a sort of “state of the industry” as it has developed over the past several months as a way of understanding its future directions and opportunities. Here we look at the major events primarily in the areas of implantable and interventional devices that are likely to shape future legal and regulatory and technical decision-making over the next several months and years. Various *sidebars* provide complementary perspectives.

**Part II** focuses on several major categories of cardiovascular illness that present the greatest threat to patients worldwide. Here the emphasis is on the major innovative technologies, and companies developing them, that attempt to deal with these problems.

In this section, we first describe the disease dynamics, then the opportunities and challenges facing the therapeutic technologies for them under development and several of the companies developing these therapies. The overview of companies includes *Updates* to indicate the progress of these technologies toward commercial approval and use, and *Notes* indicating company clinical, regulatory and financial milestones. Again, *sidebars* are used to complement this information.

**Part III** looks at key technologies that have reached maturity in cardiovascular device science and clinical practice — but continuing to provide improvements through advanced iterations and greater sophistication. These too are supplemented by *Updates, Notes* and *sidebars*.

These three parts are followed by an *Appendices* offering materials that identify other issues of interest, such as the state of cardiovascular technology in Europe and important complementary technical and regulatory information.

— DON LONG, MDD Executive Editor
Thanks, acknowledgements

Advances in Cardiovascular Technology: State of the Industry and Emerging Markets, Vol. 4, was developed from a variety of sources: material taken from AHC Media’s med-tech group of publications, including Cardiovascular Device Update, The Biomedical Business & Technology newsletter, Medical Device Daily and Diagnostics & Imaging Week; interviews with industry experts in the cardiovascular sector; company statements and web sites; and analyst reports.

We especially want to thank a group of writers from whom we have drawn material, either wholly or in part, excerpted or paraphrased: Larry Haimovitch and Michael Simonsen, PhD, contributing editors; Jim Stommen, national editor of Medical Device Daily; Holland Johnson, Medical Device Daily managing editor; Mark McCarty, Medical Device Daily Washington editor; Karen Young, Amanda Pedersen and Omar Ford, Medical Device Daily staff writers. Other important contributors were Rob Kimball and Robin Mason, providing research and production assistance.
**Glossary of key terms and acronyms**

**510(k)** — designation for those FDA marketing clearances of medical devices for which there are similar, or predicate, devices already on the market and usually indicating devices that have the lowest level of health risk in patient treatment.

**AAA, TAA** — abdominal aortic aneurysm, a ballooning of the abdominal aorta that may burst and cause fatality; thoracic aortic aneurysm.

**ACC** — American College of Cardiology (Bethesda, Maryland).

**AED** — automated external defibrillator.

**AF/Afib** — atrial fibrillation, the most common form of heart arrhythmia.

**AHA** — American Heart Association, a major U.S. association monitoring heart disease and providing advice and resources for prevention.

**angina** — discomfort due to coronary heart disease; includes pressure or pain in the chest, arms or jaw.

**angiogenesis** — development of new blood vessels.

**angiogram** — X-ray image of an artery or vein highlighted with contrast media.

**angiographic binary restenosis (ABR)** — percent of subjects with a 50% or greater stenosis of the vessel lumen after PTCA/stenting; importantly, ABR can occur without the presence of clinical symptoms.

**angioplasty** — invasive procedure in which a catheter with an inflatable balloon at one end is used to open blocked coronary arteries; technically termed percutaneous transluminal coronary angioplasty (PTCA).

**arrhythmia** — general term for any heartbeat rhythm that is abnormal. *For a list of various types of arrhythmias see Glossary of key terms and acronyms, p. 35.*

**atria** — upper chambers of the heart.

**AVM** — arteriovenous malformation, a malformed area of blood vessels where an artery feeds blood to the vein without passing through the cells first. This causes increased pressure in the vein which, over time, may lead to rupture.

**BMS** — bare-metal stent.
BNP — B-type natriuretic peptide.

CABG — coronary artery bypass grafting, an open surgical procedure for improving blood flow to the heart.

CAD — coronary artery disease.

CAE — carotid artery eee, an open surgical procedure to clear an occlusion of the carotid artery.

CAS — carotid artery stenting, a percutaneous procedure for clearing an occlusion of the carotid artery.

CHF — congestive heart failure, primarily the buildup of fluid in the body — especially the feet and lungs — as the result of late-stage heart failure which reduces the pumping ability of the heart.

CDRH — Center for Devices and Radiological Health, the unit of the FDA primarily responsible for regulating medical devices, including cardiovascular devices and radiological systems.

CE mark — designation for those medical devices cleared for marketing in the European Union, generally equivalent to FDA 510(k) clearance/PMA approval.

CMS — Centers for Medicare and Medicaid Services.

coronary arteries — arteries supplying blood directly to the muscle walls of the heart.

coronary artery disease — narrowing of the coronary arteries so that the heart muscles do not receive an adequate supply of blood.

CTA — computed tomography angiography

deliverability — the ease with which a stent can be deployed to the target location of the vasculature.

de novo — new or initially appearing.

DES — drug-eluting stent, a stent comprised of a polymer holding a drug that is intended to reduce occlusion of the artery following stent placement.

ECG/EKG — electrocardiogram, a recording of the electrical activity of the heart.

embolism — blockage in the vasculature that prevents the flow of blood and may lead to heart attack or stroke.

endovascular — describing a procedure performed using minimally invasive, catheter-directed techniques from within the blood vessel as opposed to open sur-
gery. Alternately referred to as percutaneous.


**FDA** — Food and Drug Administration, the U.S. governmental agency responsible for approving and regulating devices, drugs and biologic products.

**HDE** — humanitarian device exemption.

**ICD** — implantable cardioverter defibrillator.

**IDE** — investigational device exemption, an FDA approval for clinical trial use in a limited number of patients.

**in-stent** — within the margins of the deployed stent

**ischemia/myocardial ischemia** — deficiency of oxygen to cells or to the cells of the heart as the result of obstructed blood supply.

**LVAD** — left ventricular assist device, a heart assist device that supports the pumping action of the left ventricle of the human heart. Also see VAD.

**MACE/MAE** — major adverse cardiac event/major adverse event.

**Maze procedure** — surgical procedure involving the creation of precise incisions in the atria of the heart to interrupt and normalize abnormal heart rhythms.

**MI/AMI** — myocardial infarction, in which the oxygen supply to the heart is cut off and causes heart attack/acute myocardial infarction, and different than a heart attack caused by a disturbance of the heart’s electrical rhythm.

**MR** — mitral regurgitation

**MRI** — magnetic resonance/magnetic resonance imaging.

**neovascularization** — the creation of new vasculature pathways for increased blood supply.

**NYHA I-IV** — New York Heart Association Classes I through IV rankings of the seriousness of heart disease, IV being the most serious.

**nitinol** — an alloy of nickel and titanium often used in medical devices.

**percutaneous** — referring to minimally invasive procedures via small incisions, in contrast to open surgical procedures.

**PFO** — patent foramen ovale, a hole in the heart, usually a normal opening at birth that then closes. In some cases it does not close, causing a variety of cardiovascular problems and more associated with migraine headaches.
PMA — premarket application, the designation for those FDA marketing approvals of medical devices that 1) may have a greater level of health risk for treated patients, and/or 2) are considered fairly groundbreaking and lacking a predicate system in terms of technology and use.

PTA — percutaneous transluminal angioplasty, a procedure involving inserting a balloon catheter into a narrow or occluded blood vessel and then inflating the balloon to open the vessel.

PTCA — percutaneous transluminal coronary angioplasty, or the use of a PTA procedure to open a coronary artery.

stenosis/restenosis/in-stent restenosis — the narrowing or occlusion of a vessel/the reclosure of a vessel after it has been opened/the renarrowing of a vessel at the site of stent placement.

stent — small tube-like device that is placed in arteries to keep them open and intended to prevent restenosis, or reclogging.

stent thrombosis — clinical trial protocol defined as acute, subacute and late. Academic Research Consortium (ARC) defined stent thrombosis: acute, subacute, late, very late. Defined within three categories: 1) definite, 2) probable, 3) possible.

SVG — saphenous vein graft, a coronary bypass graft made from the saphenous vein harvested from the patient’s own body.

target lesion revascularization (TLR) — any repeat percutaneous intervention of the target lesion or by bypass surgery of the target lesion.

target vessel failure (TVF) — clinical trial protocol-defined event, including death, myocardial infarction, emergent CABG or TLR that cannot be attributed to a vessel other than the target vessel.

target vessel revascularization (TVR) — clinical trial protocol-defined revascularization of the target vessel.

thrombus — blood clot.

VAD — ventricular assist device, meaning a heart assist device that supports the pumping action of the ventricle of the human heart. Also see LVAD.

ventricles — left and right pumping chambers of the heart.

VF — ventricular fibrillation.

VT — ventricular tachycardia.