A Period of Refinement

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Quantitative coronary arteriography (QCA) is an important tool for studying the effects of coronary interventions in the catheterisation laboratory in an accurate and reproducible manner. Nowadays, peer-reviewed publications on relevant interventional trials are only accepted if the vascular interpretations are presented in quantitative terms, whereby the degree of restenosis, and the so called late lumen loss, are the most relevant parameters.

Important technical developments in the catheterisation arena over the past 15 years have included the digitisation of the catheterisation laboratories, whereby the conventional 35mm cinefilm was replaced by the digital CD. Furthermore, the image data is now stored in digitial imaging and communications in medicine (DICOM) format. This greatly simplifies the transfer of the image data on digital copies to other physicians and the imaging core laboratories (ICLs), where they can be analysed without any loss of information. In the last few years, an increasing number of cardiovascular X-ray imaging systems have been equipped with flat-panel detectors, replacing the conventional vacuum tube image intensifier in combination with a CCD camera. There are a number of major advantages to these flat-panel detectors, which include the ability to preserve significantly more of the original digital signal and the absolute absence of spatial distortions thereby providing superior image quality and enabling further image enhancement. In clinical practice, this means improved visibility of vessels, lesions, stents and guidewires, even at reduced X-ray dose levels.

The great advantage of a QCA analysis is that the sizes of the selected coronary segments can be determined from the coronary arterial arteriograms in a standardised manner according to standard operating procedures (SOPs) with robust and automated contour detection techniques. A typical example of a QCA analysis in a circumflex artery is given in Figure 1. The most relevant parameters are the minimal lumen diameter (0.58mm) of the obstruction, the reference diameter (2.06mm), the percentage diameter stenosis (71.96mm) and the length of the obstruction (9.82mm). These techniques were first introduced in the early 1980s and have been further improved, extended and extensively validated since then (1,2). Important new interventional developments over the past 10 years have been the use of brachytherapy, drug eluting stents (DES) and bifurcation stenting, which have required special analytical options to be developed for these applications. Also, interventions in peripheral vessels, such as the carotid arteries, renal and femoral arteries, have received increased interest. These applications will be described briefly in the following paragraphs.

BRACHYTHERAPY

Brachytherapy was introduced in an attempt to treat in-stent restenosis. The angiographic evaluation of brachytherapy trials is much more challenging than standard QCA due to the extent of the segment receiving therapy (up to 60mm in length) and the multiple associated landmarks (lesion, balloon injury, stent and radiation device) that need to be carefully tracked from the baseline angiogram to the angiograms after final intervention, and at follow-up a number of months later (3). The recurrent stenosis may theoretically occur at any location within either the stent, the segment of balloon injury, of the radiation delivery

device, or within its dose fall-off zones. To further describe the inter-relation of radiation delivery and the extent of vascular injury, three additional zones are routinely defined within the special brachy-QCA option within the software: geographic hit, geographic extension and geographic miss segments. It will, therefore, be appreciated that these complex analyses require a superior knowledge of the anatomy and the process of restenosis, and require the dedicated attention of the core lab technician when performing such analyses to ensure precise and accurate results in the clinical trial.

DRUG ELUTING STENTS

Drug eluting stents (DES) were introduced in the early years of this millennium; in April 2003 the first drug eluting stent became commercially available in the US. The expectation was that by combining the advantages of a stainless steel scaffold with the controlled release of an antiproliferative agent modulated by a polymeric coating, the most important problem after PCI would be reduced. Nowadays, two platforms have been approved for clinical usage and research, the Sirolimus (Cypher, Cordis/Johnson & Johnson, Warren, New Jersey) and Paclitaxel coated stents (Taxus, Boston Scientific, Natick, Massachusetts) (4,5). Various studies have shown that both DES devices more efficiently prevent angiographic and clinical restenosis rates compared with bare-metal stents. There have been concerns that significant restenosis would occur in juxtaposition with the stents, and at those locations where the vessel was dilated, but not stented. To quantify the possible effects, the standard QCA software had to be developed with additional features allowing these further detailed analyses. A good example of restenosis within the 5mm range outside of the DES stent is given in Figure 2, where a restenotic lesion with a 33.45 per cent diameter stenosis was found at six month follow-up at a distance of 4.96mm from the distal stent edge in a left anterior descending artery (LAD).

In addition to QCA, intravascular ultrasound (IVUS) has allowed the development of a quantitative benchmark for acceptable late loss post-DES stent implant. This reduction in late loss has translated in dramatic reductions in clinical restenosis. QCA also allows accurate assessment of lesion length. Adequate coverage of index lesion site with stent implantation is essential in reducing restenosis and minimising an untreated edge effect. It is therefore anticipated that future stent trials will continue to incorporate QCA into the trial design to predictably measure the vascular healing response following stent implant.

EXTENSIONS TOWARDS BIFURCATION ANALYSES

Now that the treatment of straight vessel segments with bare metal and drug-eluting stents have become standard procedures in the catheterisation laboratories, the next step in the evolution of interventional cardiology, has been the treatment of bifurcation lesions (6). Various techniques are being developed to find out which is the best approach to deliver the two stents, one in the main branch and the other one in the side branch. It has been well known that arterial branch points are areas of low flow and low shear rates, and therefore predisposed to the development of atherosclerotic plaque. It is clear that separate QCA analyses of the main stem and the two side branches by the standard straight

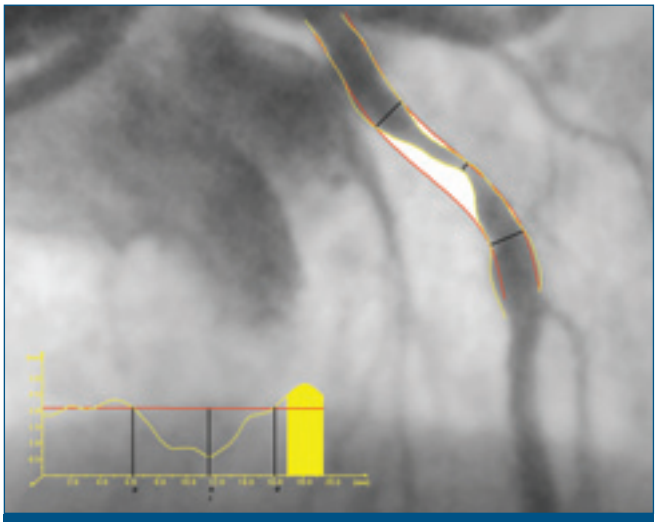

Figure 1: Typical example of QCA analysis in a straight vessel segment – in this case a circumflex artery. QCA parameters are: obstruction diameter 0.58mm, interpolated reference diameter 2.06mm, the derived diameter stenosis71.96%, and obstruction length 9.82mm

vessel analyses create some problems in the sense that the bifurcation lesions and their lengths cannot be properly described, and that for lesions distally at the bifurcation overestimations of the reference diameter usually occur. To resolve these problems, special QCA bifurcation and ostial segment analytical approaches have been developed. Figure 3 shows a good example of a bifurcation analysis of a lesion in the LAD artery. In this case, the reference diameter (2.64mm) was not overestimated as a result of the special algorithms developed. Validation studies have clearly demonstrated that this new method for the analysis of bifurcation lesions eliminates the overestimation of the percentage diameter stenosis, and that the reproducibility is similar to the established ones for the straight vessel analyses (7).

EXTENSIONS TOWARDS VASCULAR ANALYSES: QUANTITATIVE VASCULAR ARTERIOGRAPHY (QVA)

Following the great success of coronary stenting, peripheral interventions have increased as well, with vessels of interest predominantly being the carotid artery, the renal artery and the femoral arteries. Nowadays, the same analytical software packages

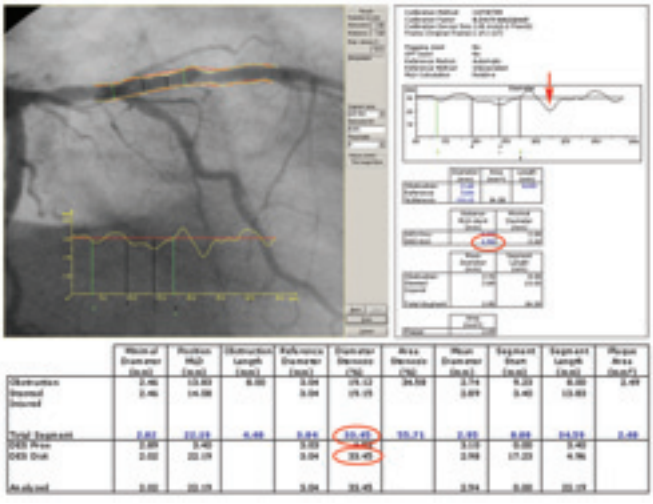

Figure 2: Restenosis at 4.96mm from the distal edge of a drug eluting stent in a LAD-artery; the diameter stenosis is 33.45%

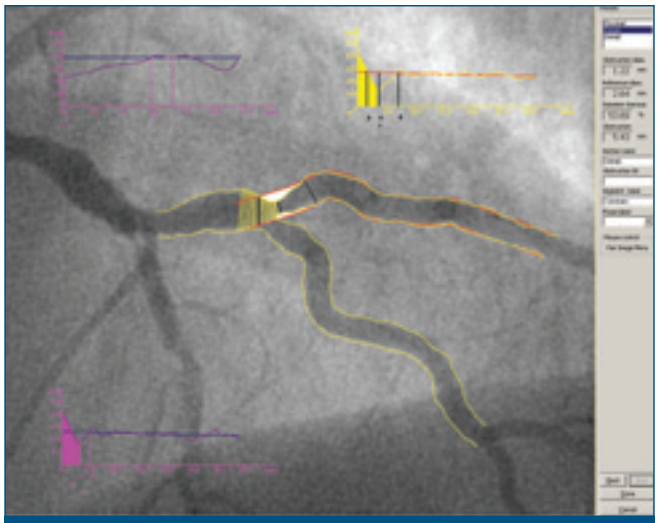

Figure 3: Bifurcation analysis of a narrowing within the bifurcation area of the left main stem and the LAD and circumflex arteries. The QCA parameters are: obstruction diameter 1.22mm, reference diameter 2.64mm and diameter stenosis 53.69%

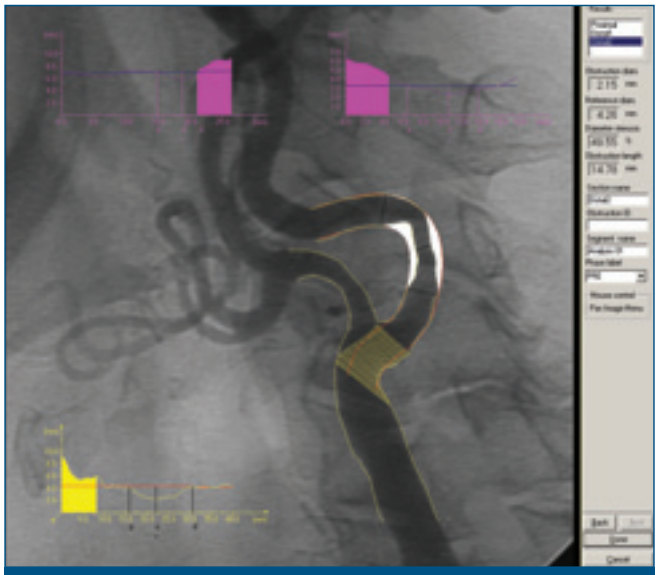

Figure 4: Example of a QVA bifurcation analysis of an obstruction in an internal carotid artery

can be used for both coronary and peripheral vessels. This analysis technique was developed in Leiden and subsequently a validation study was carried out to assess the variability (8). A typical example of a carotid artery analysis is demonstrated in Figure 4. In the validation study, a total of 51 pre-treatment angiograms of the internal carotid artery were analysed twice, with a three-week interval by three different observers. The target lesions were all located in the internal carotid artery or partly in the bifurcation. It was concluded that the inter- and intra-observer variability in quantitative vascular analysis (QVA) analysis is low (<0.18mm for intra and <0.27mm for inter) when using the interpolated reference diameter method and by strict application of SOPs at the core lab. From these data, new guidelines for QVA in clinical trials were derived, setting a new standard for the future, and requiring fewer patients in clinical trials.

QVA is routinely utilised in the assessment of carotid artery reference size to allow appropriate selection of filter protection device and carotid stent diameter selection. In order to ensure complete cerbrovascular protection, the distal protection device (that is, a filter) must be of accurate diameter to have complete opposition in the arterial lumen. QVA also allows the assessment in tortuous carotid circulation.

CONCLUSION

QCA has changed dramatically in the last few years, in part with the advent of new stents and methodologies. The requirements for assessing the efficacy of these new technologies have continued to push the development of new analysis tools to allow the precise quantification of the devices and drugs. The ability to treat patients with drug eluting stents that only a few years ago would have been considered experimental has in part been attained due to the new image acquisition and analysis techniques which have been refined at the imaging core labs. With the rapid advancement of these techniques in recent years, one can only speculate as to the further advancement that might occur over the coming years. ◆

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