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Vessel-Specific Quantification of Absolute Myocardial Blood Flow, Myocardial Flow Reserve and Relative Flow Reserve by means of Fused Dynamic $^{13}\text{NH}_3$ PET and CCTA: Ranges in a Low-risk Population and Abnormality Criteria.

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Abstract

Objectives.—The goal of the present work is to present a novel methodology for the extraction of MBF, MFR and RFR along coronary arteries by means of multimodality image fusion of dynamic PET and CCTA images.

Background.—FFR is the reference standard to identify flow-limiting lesions, but its invasiveness limits broad application. New noninvasive methodologies are warranted to stratify patients and guide treatment.

Methods.—A group of 16 low-risk CAD subjects who underwent both $^{13}\text{NH}_3$ PET and CCTA were analyzed. Image fusion techniques were employed to align the studies and CCTA-derived anatomy used to identify coronaries trajectories. MBF was calculated by means of a 1-tissue compartmental model for the standard vascular territories and along patient-specific vessel paths from the base to the apex of the heart.

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Conflict of Interest Disclosure

Some of the authors (EVG, RDF, CDC) receive royalties from the sale of the Emory Cardiac Toolbox and have equity positions with Syntermed, Inc. The terms of these arrangements have been reviewed and approved by Emory University in accordance with its conflict of interest policies. The remaining authors did not report any conflicts of interest.

Results.—Low-risk ranges for MBF, MFR and RFR for LAD, LCX and rPDA were computed for the entire cohort and separated by gender. Computed low-risk ranges were used to assess a prospective patient with suspected CAD.

Conclusions.—Our vessel-specific functional indexes and 3D displays offer promise to more closely replicate what is commonly performed during a catheterization session and have the potential of providing effective noninvasive tools for the identification of flow-limiting lesions and image-guided therapy.

Introduction

Recent clinical trials¹ on the assessment of CAD and therapy guidance have shown the importance of identifying flow-limiting and ischemia-provoking lesions prior to intervention. Invasive FFR has emerged as an index capable of separating lesions that will benefit from revascularization from those that should be medically treated². While FFR presently represents the standard to validate new imaging techniques or procedures that aspire to guide treatment, its invasiveness limits its application to broad populations.

Cardiac PET³ with its ability to estimate MBF, MFR and RFR^{4,5} - a proxy for FFR⁶ - has been shown to noninvasively provide quantification of the physiologic significance of CAD. Additionally, we⁷ and others⁸ have shown that fusing relative MPI to CCTA images results in improved diagnostic performance when assessing CAD.

The aim of this work is two-fold. First, for the first time, to noninvasively quantify low-risk myocardial absolute flow and derived physiological indexes, such as MFR and RFR, *from the base to the apex of the LV along specific vessels* by fusing dynamic PET images to CCTA. Second, to demonstrate by a clinical example the feasibility of the proposed methodology in detecting flow-limiting lesions.

Methods

Patients Population and Imaging Data

In this retrospective study, imaging data from a group of 16 subjects with *low-risk of CAD* (LRC) enrolled from two international collaborating centers were analyzed. Six cases were collected at Chonnam National University Hospital (Republic of Korea) and 10 cases at the Instituto Nacional de Cardiología Ignacio Chavez (Mexico). The subjects were selected from larger databases of patients who underwent a two imaging-modality examination comprised of a rest/stress (r/s) ¹³NH₃ PET study and a CCTA. The studies were approved at each institution by local IRB committees and written informed consent was obtained from all subjects.

Inclusion criteria for the selected LRC group were negative results for both the relative myocardial perfusion test, evaluated in terms of SSS, and the anatomical assessment with CCTA, performed with the semi-quantified CAD-RAD scoring system⁹ that labeled major vessels and side branches on a scale of 0 (no plaque) to 5 (100% occlusion). Patients had no prior history of CAD, myocardial infarction or revascularization; standard clinical information was also collected for all analyzed subjects.

Imaging data for one patient with suspected CAD that underwent ICA was provided by collaborators at Seoul National University Hospital (Republic of Korea).

PET Protocols and Acquisitions

All centers followed equivalent r/s PET clinical protocols. Patients were asked to fast overnight and abstain from using caffeine-containing beverages for 24 hours prior to the test and vasodilator medications were stopped. Before the resting study, a single low-dose CT-based transmission scan was acquired for AC of all subsequent acquisitions. R/s perfusion images were acquired after intravenous injection of a single bolus of $^{13}\text{NH}_3$; hyperemia was induced at all centers by 6-min adenosine infusion (140 $\mu\text{g/kg/min}$) through a peripheral vein. All PET images were ECG-gated and acquired in list mode.

CCTA Protocols and Acquisitions

ECG-gated CT acquisitions were acquired according to clinical guidelines. Sixty mL of nonionic contrast agent were injected at a rate of 4 mL/sec. The best diastolic phase was selected for successive processing.

All CCTA images were interpreted by a CT expert and results provided with CADRADS standardized reporting system.

ICA Protocol and Functional Measurements

Coronary angiography was performed according to standard techniques and guidelines. Best angiographic views and all measured functional parameters were transferred to Emory University for further analysis.

PET-derived MBF and MFR: Global Regional and Standard Measurements.

Standard software tools were used for the analysis and quantification of relative MPI¹⁰. The quantification of r/s MBF was performed by means of 1-tissue compartmental model (CM). The methodology is briefly here summarized. A late summed image was created from each dynamic acquisition with data from the second half of acquisition interval and used to identify volume of interest (VOIs) for the LV and the standard vascular territories (LAD, LCX, RCA). Time activity curves (TACs) were derived by sampling dynamic images on the segmented regions. The arterial input function (AIF) was measured from a spherical region with a diameter of 5 mm centered at a local maximum within the left atrium. TACs and AIF were used as input data to the CM that included corrections for spill-over, partial volume (PVE), and finite resolution effects. The 6 parameters of the model were: k_1 , tissue blood volume (0.05), recovery coefficients for the blood and tissue, and spillover from blood to tissue (0.95) and tissue to blood (0.8). The tissue blood volume and spillover coefficients were fixed as indicated; the other three parameters were determined from a fit with a least-squares figure of merit. Flow values was corrected from the resulting k_1 by using the Renkin-Crone model with $\text{PS} = 2.34$. Figure 1A depicts the steps from the images to the flow estimation for a stress test of one of the analyzed cases. The rate-pressure products (RPP) were monitored to account for variability in hemodynamics responses during resting and hyperemia.

MBF and MFR are often computed without considering slices from the basal segments due to PVE concerns¹¹. Thus, MBF and MFR have been calculated for LV, LAD, LCX and RCA with and without basal segments to estimate the impact of basal segments removal on flow calculation. Basal segments were objectively defined as segments 1 – 6 from a standard 17 segment LV model. MBF values were normalized by means of rest and stress RPP according to the following equations¹¹:

$$\begin{aligned}\text{stress MBF}^{\text{corrected}} &= (\text{stress MBF}^{\text{uncorrected}}/\text{RPP}) * 10000 \\ \text{rest MBF}^{\text{corrected}} &= (\text{rest MBF}^{\text{uncorrected}}/\text{RPP}) * 6000\end{aligned}$$

CCTA-derived Anatomy: Myocardium and Coronary Arteries.

CCTA images were manually segmented by means of in-house developed software to extract the myocardium and the centerlines describing patient-specific coronary trajectories. A 3D biventricular model of the heart and coronary centerlines were derived with standard image processing techniques. For each vessel, the portion of myocardium subtended to its course was extracted by creating a *column of contiguous volumetric elements* within the myocardium thickness that followed the 3D centerline from base to apex. Figure 2 describes the series of fully-automated steps performed to generate the vessel-specific VOIs successively used to sample the PET data. Two user-defined parameters (*width* and *length*) were chosen to generate the volume samples and set to 6 and 4 mm respectively. In Figure 2C vessel-specific VOIs for all visible vessels are depicted for one analyzed case.

The CCTA-derived anatomy of the myocardial tissue allowed the measurements of the heart dimensions, blood chambers volumes, myocardial mass and regional thickness.

CCTA/dynamic PET Image Fusion and Vessel-Specific MBF, MFR and RFR Quantification.

After PET/CCTA images were co-registered using our image fusion⁷ technique, all the volumetric elements within the myocardium subtended to each coronary were used as new stand-alone VOIs to sample the dynamic PET and obtain vessel-specific TACs. Once used as additional inputs to the CM, estimated r/s MBF values were returned at each element location along the centerline, providing the MBF profile along the vessel from base to apex. In Figure 1B (right panel) the steps for the vessel-specific MBF quantification are depicted for the LAD. The fusion procedure allowed to co-localize anatomy and perfusion and extract vessel-specific TACs underneath the vessel. MBF was computed for each volumetric element and plotted as a function of the distance in mm from the base (Figure 1B bottom). Vessel-specific MFR and RFR were also defined as a function of the distance from the base as the point-by-point ratio of respectively stress over rest MBF and stress MBF over highest hyperemic flow value computed on the standard vascular territories⁵.

While the technique could be applied to any visible vessel, we focused our analyses to the definition of r/s MBF, MFR and RFR low-risk ranges for the main vessels supplying the LV: LAD, LCX and rPDA. Profiles for each vessel type were normalized to their length and averaged to obtain mean r/s MBF 2D plots; at each sampling location from the base to the apex, the lowest flow value was used to identify the lowest normal range for the vessel under study. The same analysis was conducted separately for the male and female subgroups in our

cohort. In addition to vessel-specific 2D plots, 3D display of anatomical structures color-coded with functional variables were also developed, namely centerline color-coded with r/s MBF, MFR, RFR.

Statistical Analysis

Continuous variables are presented as mean $\pm$ SD, while discrete variables were expressed as frequency and percentages. Analyses were performed for the entire cohort and separately for male and female subjects. The mean differences in conventional MBF, MFR and RFR were tested by two sample 2-sided Student t-test.

Results

Study Cohort Characteristics

Patients demographic data and distribution of CAD risk factors are given in Table 1. Average PET-derived SSS was 1.9 for the entire cohort and 1.8 and 1.9 respectively for the female and male groups. The Framingham risk score was computed to assess risk of cardiovascular disease and was 7.8 ± 9.6 globally, 1.6 ± 0.8 and 10.6 ± 2.9 for respectively female and male groups. One significant stenosis (DS >70%) was identified on the CCTA along one LAD vessel, which was removed from all analysis. All remaining cases showed no evidence of CAD disease or minimal irregularities (DS<24%). Table 1 reports the hemodynamic responses measured during PET studies exhibiting statistically significant differences in the rest RPP between male and female groups.

Anatomy Extraction

For all CCTA images, myocardial tissue and coronary artery centerlines were extracted; LV and RV chambers volumes, left myocardial mass and thickness computed (Table 2). Both LV myocardial mass and RV volume showed gender-based significant differences ($p<0.05$). The mean myocardial thickness increased from apical to mid to basal region; it was consistently smaller for the female group in all regions and significantly different at the apex.

All the coronary arteries visible on CCTA images were reconstructed in terms of centerlines. The number of arteries that could be modeled varied among cases: all LADs, rPDAs and a major vessel supplying the LCX territory were always visible; a variable number of side branches were also modeled.

MBF Quantification

Automated standard analysis of r/s PET acquisitions was performed with ECTb¹⁰. The mean $\pm$ SD for r/s MBF and MFR for all cases and separately analyzed by gender are shown in Table 3. The removal of basal segments consistently and significantly ($p<0.01$) increased r/s MBF and MFR for the entire LV and individual territories (p-values not shown in Table 3). When separated for gender and within each approach – i.e. with and without basal segments – significant differences were consistently found for all resting MBFs and for hyperemic MBF in the RCA territory (Table 3). MFR values showed no significant differences. The significant differences disappeared when resting flow values were corrected by means of

RPP. The distribution of r/s MBF separated by gender are depicted for LV, LAD, LCX and RCA in Figure 3 with all segments (A) and without basal segments (B).

Image fusion was successfully performed for all cases. The correctness of the fusion procedure was visually assessed on 3D displays for the fused imaging datasets and for 3D models of PET- and CCTA-derived surfaces of anatomical structures. Vessel-specific MBF, MFR and RFR profiles from the base to the apex were computed for the LAD, LCX and rPDA vessels and averaged to obtain low-risk ranges. In Figure 4 r/s MBF, MFR and RFR are depicted for the analyzed vessels for the entire cohort. In Figure 5 results are separated for male and female. Despite noticeable differences in male versus female flow values, from Table 3 statistical significances were found for all resting flows and only the sMBF of the rPDA territory. Lack of statistical sMBF differences between gender in the LAD and LCX territory were mostly due to the large standard deviations in the female mean flow values. R/s MBF profiles commonly exhibited a “bell shape” with values increasing from proximal to mid-myocardial locations and decreasing towards to apex. This is particularly evident for LAD and rPDA, less for the LCX as vessels supplying this territory can rarely be tracked all the way to the apex due to their rapidly tapering dimensions.

An example of 3D rendering of anatomy and flow quantifications for all visible vessels in terms of color-coded centerlines is shown (Fig 6) for stress and rest MBF of one of the low-risk analyzed cases.

Application of our proposed methodology is illustrated for the case of a female 46 yo patient with suspected CAD (Figs 7, 8). Polar maps of conventional relative perfusion revealed a large defect on the mid anterior and apical regions. The patient also exhibited normal rMBF, decreased stress MBF across all territories and decreased MFR in the LAD territory (rMBF: 0.76, 0.76, 0.76 mL/min/g; sMBF: 1.31, 1.70 and 1.71 mL/min/g; MFR: 1.73, 2.24 and 2.24. Vessel-specific flow quantification was performed for all reconstructed vessels (Figure 7A). Abnormality of r/s MBR, MFR and RFR along the vessels length was interrogated by comparison to our low-risk ranges in 2D plots. In particular the LAD flow quantification showed reduced sMBF and MFR although above our lowest limits (Figure 7B); the vessel-specific RFR remained above our lowest threshold for the entire length of the vessel (Figure 8B). The LCX and rPDA showed normal r/s MBF, MFR and RFR (data not shown). The patient was sent to catheterization lab and the LAD investigated: FFR and instantaneous wave-free Ratio (iFR) were respectively 0.73 and 0.87 (Figure 8 A, D). A direct comparison of our PET-derived RFR plot and the invasive FFR pullback is shown in Figure 8B and 8D, which exhibit a relatively good agreement between the non-invasive measure and the one obtained during invasive catheterization. In Figure 8C a 3D rendering of the PET-derived RFR is displayed.

Discussion

In the present work, a novel methodology was introduced for the extraction of MBF, MFR and RFR along vessel-specific trajectories by means of multimodality image fusion of r/s dynamic PET and CCTA. By means of our recently validated 2nd generation image fusion techniques⁷, we strengthen our approach by moving from relative to absolute quantification

of myocardial perfusion. Our vessel-specific functional indexes and 3D displays can more closely replicate what is commonly performed during a catheterization session and have the potential of providing effective noninvasive tools for the identification of flow-limiting lesions and image-guided therapy.

This is the first time that anatomy-guided measurements of coronary physiology (r/s MBF, MFR, RFR) have been noninvasively estimated by means of PET as a function of the distance from the base along the artery. The concept of measuring the radiotracer activity gradient from base-to-apex along the LV long axis was previously introduced¹². Relative tracer concentrations were measured on each image slice from base-to-apex on different LV quadrants and for different patient populations from normal to severely diseased. The authors described the ability of their methodology to capture progressive abnormalities in tracer concentrations in the longitudinal direction even in cases of diffuse disease without perfusion defects. Analogously in more recent investigations¹³, gradient hyperemic MBF from the mid to the mid-to-apical sections of the LV was used to detect the presence of initial CAD and/or the hemodynamic significance of epicardial stenosis. In all these investigations though, MBF estimations rely on standard partition of the LV into territories. Yet coronary anatomy can be significantly different among patients¹⁴ and final flow values may result from intermixing data from normal and abnormal tissues, a shortcoming that equally affects standard MBF quantification. The inclusion of CCTA-derived anatomical information allowed our base-to-apex measurements to sample the myocardium beneath the vessels, potentially increasing our ability of detecting local flow deficiencies, linking them to epicardial lesions and directing treatment. The use of fused data obtained by means of hybrid PET/CT to detect hemodynamically significant lesions by means of MBF quantification was described by Kajander et al¹⁵. Their proposed methodology allows a visualization of the MBF map values with superimposed anatomy via volume rendering techniques showing excellent diagnostic accuracy when compared to FFR.

Our methodology was here applied to a cohort of LRC patients to define low-risk ranges of vessel-specific indexes and used to test the methodology feasibility in one abnormal patient.

Standard and Vessel-Specific Flow Quantification and Comparison to previous Studies

Several reports have been published determining ammonia normal rest MBF, stress MBF and MFR including compendiums of reported values, most notably Murthy's compendium¹⁶ which included 23 articles determining normal flow values with a combined sample size of 363. Most of these reports used normal healthy volunteers with an average age of 37.6y. We chose to use actual patients with average age of 68y referred to either PET or CCTA. Once the first study was interpreted as normal, the second study was performed as part of this investigation. As the understanding of the variables that affect MBF improves, it has become more difficult to define what constitutes an age-matched patient with "normal" MBF and no risk factors. Thus, we chose to study a low-risk population as determined by their Framingham score (7.8) and confirmed by CCTA and PET reported thresholds for normal flow. Our sample size is similar or larger than in 15 of the 23 articles in Murthy's compendium¹⁶. The average of our global LV flow results compared favorably with the compendium: rest MBF (0.70 vs. 0.71), stress MBF (2.59 vs. 2.58) and MFR (3.84 vs. 3.54).

We also found significant gender differences in resting MBF with females having larger values¹⁷.

What separates our work from other reports is that for the first time we used a low-risk, age-matched population to determine average flow values and ranges (including RFR) in the myocardial tissue just below the three major epicardial coronary vessels as depicted in Figure 1 and 2. LAD, LCX and rPDA were here analyzed as the main vessels supplying the LV, but our methodology is applicable to any vessel whose trajectory is visible at CCTA. The base-to-apex profiles consistently showed a common pattern: increasing values at the base that peak at mid-LV and gradually decrease towards the apex. PVE from true myocardial thickness may play a crucial role in these results. The equations at the base of common tracer kinetic modeling techniques assume a constant value throughout the entire LV, altering the reliability of results in locations where this assumption is less valid. By way of CCTA-derived anatomy we measured myocardial thickness that progressively increased from the apex to the base, trending differences between male and female subjects (Table 2). These findings represent the rationale for the common removal of basal segments from standard MBF calculation, a procedure that - as described in this work - can have a significant impact on final flow calculation (Table 3). A major future development for our methodology will be the inclusion in our flow calculations of regional recovery coefficients determined from the true LV myocardial thickness by means of CCTA.

The motivation behind the definition of any normal database is its usage as a reference to stratify abnormal cases. As *proof of concept* and to attest the methodology's technical and clinical feasibility, we analyzed a patient with suspected CAD with our approach and used our vessel-specific LRC ranges to evaluate the presence of hemodynamic deficiencies along main vessels. The LAD was specifically investigated in the catheterization lab by means of FFR and iFR; the patient was ultimately not treated. In Figure 7 and 8 our noninvasive quantification of the LAD is provided in terms of 2D and 3D displays. Interestingly, the base-to-apex LAD sMBF and MFR were borderline normal, but with RFR that remained within LRC ranges, underlining the potential of these indexes to depict different aspects of CAD disease. This specific clinical scenario is described in a recent work by Dr. Lee and colleagues⁵. These authors stratified lesions characterized by abnormal sMBF and MFR according to RFR value into epicardial disease (RFR<0.80) and diffuse epicardial disease and/or microvascular disease (RFR>0.80). Our results suggest to a non-significant lesion, probably coupled with microvascular dysfunction, thus the decision not to treat. A compelling product of our methodology, as shown in Figure 8 where ICA findings are shown, is its potential to perform a direct comparison of lesion location and physiological significance between invasive and non-invasive measurements.

Limitations of our present methodology.

The proposed methods represent a proof-of-principle of the potential to non-invasively measure myocardial flow parameters to determine the location, significance and characteristic (epicardial vs. microvascular or diffuse) of coronary pathophysiology. The sample size for the creation of normal ranges was limited (n=16), although similar to previous publications that reported MBF normal ranges¹⁶. One single clinical patient with

suspected CDA was presented to show the potential of our methodology in clinical settings. A comprehensive validation is necessary and will require a properly powered, prospective, and appropriately characterized patient database. Thus, clinical implementation of the approach is the major limitation of the present work.

Furthermore, the myocardium and the coronaries centerlines were manually outlined, a task that can become time consuming and thus making the present approach impractical. Our team has actively been working in the development of automated techniques. This automated methodology was previously tested on an animal model¹⁸ and is presently being validated in a large database of CCTAs. As only vessel centerlines are required, there are number of approaches available to automate this step¹⁹.

A common criticism to the multimodality approach is the radiation burden associated with a dual-modality strategy. Technological improvements on the latest devices and new protocols have partially mitigated this concern. In the context of nuclear MPI, PET has a lower radiation dose than SPECT, while a good quality clinical CCTA can be acquired today with a radiation dose < 1mSV.

Conclusions

We developed a novel methodology to extract noninvasively and in a vessel-specific fashion r/s MBF, MFR and RFR base-to-apex of the LV by means of PET/CCTA multimodality image fusion. The application of this approach to a cohort of low-risk patients results in the definition of acceptable clinical ranges for coronary physiology for the LAD, LCX and rPDA. These low-risk ranges can be prospectively used as reference to potentially assess noninvasively lesions location and significance by means of functional indexes that more closely reproduce what is commonly performed and measured during catheterization sessions.

New Knowledge Gained

Vessel-specific profiles of rest and stress MBF, MFR and RFR from the base to the apex of the heart following patients' coronary trajectories may be extracted and compared to their low-risk ranges to potentially determine coronary pathophysiology. The base-to-apex mean low-risk flow profiles exhibited increasing values from the base to a mid-LV peak that gradually decreased towards the apex. Significant differences in resting flow exist between the low-risk male and female populations (females higher values) as well as between flow values that included the basal segments and those that did not (without basal segments higher). Significant differences also exist between low-risk males and females in RV volume, LV mass and LV thickness (men higher).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

CAD	Coronary Artery Disease
CCTA	Coronary Computed Tomographic Angiography
ECG	Electrocardiogram
FFR	Fractional Flow Reserve
HR	Heart Rate
ICA	Invasive Coronary Angiography
LAD	Left Anterior Descending Artery
LCX	Left Circumflex Artery
LV	Left Ventricle
MBF	Myocardial Blood Flow
MFR	Myocardial Flow Reserve
MPI	Myocardial Perfusion Imaging
PET	Positron Emission Tomography
RCA	Right Coronary Artery
rPDA	Right Posterior Descending Artery
RFR	Relative Flow Reserve
SBP	Systolic Blood Pressure

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Figure 1. Procedures for PET-derived MBF estimation. A) Standard Quantification (from top to bottom): identification of standard vascular territories and AIF on a 3D display of a summed image; TACs are extracted for LAD, LCX, RCA and AIF, and used as input data into the CM; displays of sMBF on a conventional polar map. B) Vessel-specific quantification: identifications of vessel-specific VOIs for the LAD centerline (red) on fused display of PET/CCTA (samples 1, 6 and 11 along the centerlines are labeled as examples); TACs from all the elements and the AIF are input data to the CM; sMBF is computed for each vessel-specific VOI and plotted as a function of the distance from the base to the apex in mm.

Figure 2. Identification of VOIs along 3D coronaries trajectory for one of the analyzed cases. A) projection of LAD centerline (red) on the epi-, endocardial surfaces (black); a mid-wall centerline (blue); B) creation of a column of contiguous volumetric elements within the myocardium; C) anterior and posterior view of one analyzed case showing vessel-specific VOIs.

Figure 3. Distribution of r/s MBF for LV, LAD, LCX and RCA analyzed for male and female groups (* indicates $p < 0.05$); solid lines represent mean MBF. A) All segments included; B) basal segments excluded from calculation.

Figure 4. Low-risk mean and ranges of vessel-specific r/s MBF, MFR and RFR from base to apex for LAD, rPDA and LCX for entire cohort. Mean (red) and lowest value (dot).

Figure 5. Low-risk mean and ranges of vessel-specific r/s MBF, MFR and RFR from base to apex for LAD, rPDA and LCX for male and female groups. Mean profiles (red (female) and blue (male)); lowest values (dashed (female) and dot (male)).

Figure 6.
3D display of CCTA-derived heart model with coronaries color-coded with PET-derived r/s MBF from a low-risk patient. Black and blue low MBF values at the base of the LV are artifactual due to total (black) or partial absence of myocardial sampling.

Figure 7.
A) 3D display of sMBF and MFR for clinical example. B) the 2D plots of vessel-specific quantification of patient's LAD (blue) compared to LRC ranges for MBF and MFR base-to-apex in mm.

Figure 8.

Assessment of lesions hemodynamic significance along the LAD in clinical example. A) ICA LAD view; B) Base-to-apex profile of RFR along the LAD (blue) compared to LRC values (red); C) Invasive FFR pullback (yellow); graph was *reversed* to match proximal-to-distal direction of measurement of RFR; D) 3D anatomic display of RFR. Red arrow indicates location of invasive measurements (FFR=0.73, iFR=0.87). Green arrows approximately show same anatomical location in panel A, B and D.

Table 1.

Patients Demographic and Hemodynamics.

	ALL	FEMALE	MALE
<i>n</i>	16	5	11
<i>Age</i>	66 ± 7	64 ± 8	67 ± 6
<i>Body Mass Index</i>	25 ± 3	26 ± 4	25 ± 3
<i>Coronary Calcium Score</i>			
=0	10 (62%)	4 (80%)	6 (55%)
< 100	3 (19%)	1 (20%)	2 (18%)
> 400	3 (19%)	0	3 (27%)
<i>Framingham Risk Score</i>	7.8 ± 9.6	1.6 ± 0.8	10.6 ± 2.9
<i>Diabetes Mellitus</i>	4 (25%)	1 (20%)	3 (27%)
<i>Hypertension</i>	11 (69%)	4 (80%)	7 (64%)
<i>Hyperlipidemia</i>	9 (56%)	4 (80%)	5 (45%)
<i>Smoking</i>	7 (44%)	2 (40%)	5 (45%)
<i>Rest Heart Rate</i>	67 ± 12	78 ± 8 *	62 ± 9 *
<i>Rest Blood Systolic Pressure</i>	123 ± 11	124 ± 5	123 ± 13
<i>Rest Rate-Pressure Product</i>	8253 ± 1594	9638 ± 895 *	7561 ± 1414 *
<i>Stress Heart Rate</i>	73 ± 13	80 ± 13	69 ± 12
<i>Stress Blood Systolic Pressure</i>	121 ± 8	126 ± 6	119 ± 9
<i>Stress Rate-Pressure Product</i>	8857 ± 1930	9978 ± 1410	8297 ± 1965

* male/female comparison p<0.05

Table 2.

CTA-derived Anatomy

	ALL	FEMALE	MALE	p-value (male vs female)
<i>CCTA-derived Myocardial Masses and Thickness</i>				
<i>LV Volume [mm³]</i>	69.0 ± 18.4	69.8 ± 23.0	68.4 ± 15.8	NS
<i>RV Volume [mm³]</i>	97.2 ± 23.5	80.4 ± 20.3	109.8 ± 17.6	< 0.05
<i>LV Myocardial Mass [g]</i>	113 ± 25.0	97.6 ± 10.0	124.7 ± 27.1	< 0.05
<i>LV Thickness [mm]</i>				
<i>apical</i>	7.68 ± 1.51	6.64 ± 0.97	8.47 ± 1.39	< 0.05
<i>mid</i>	9.94 ± 1.97	9.01 ± 1.78	10.64 ± 1.91	NS
<i>basal</i>	11.47 ± 1.94	10.44 ± 1.39	12.25 ± 2.0	0.08

NS = non-significant

Table 3.

MBF and MFR calculated for the LV and the standard vascular territories with and without basal segments, for all cases and separated by gender.

<u>All Segments</u>											
LV			LAD			LCX			RCA		
rest	stress	MFR	rest	stress	MFR	rest	stress	MFR	rest	stress	MFR
0.70 ±0.21	2.59 ±0.88	3.84 ±1.18	0.68 ±0.19	2.64 ±0.97	3.95 ±1.21	0.75 ±0.25	3.28 ±1.53	4.53 ±2.08	0.65 ±0.21	2.14 ±0.58	3.37 ±0.76
0.61 ±0.07	2.37 ±0.72	3.93 ±1.16	0.60 ±0.07	2.48 ±0.71	4.12 ±1.09	0.66 ±0.10	2.96 ±1.42	4.57 ±2.14	0.56 ±0.07	1.91 ±0.45	3.42 ±0.76
0.89 ±0.29	3.09 ±1.07	3.65 ±1.33	0.85 ±0.25	2.98 ±1.42	3.58 ±1.52	0.97 ±0.34	3.98 ±1.68	4.43 ±2.17	0.85 ±0.29	2.63 ±0.57	3.25 ±0.83
p<0.01	NS	NS	p<0.01	NS	NS	p<0.05	NS	NS	p<0.01	p<0.05	NS
<u>No Basal Segments</u>											
LV			LAD			LCX			RCA		
rest	stress	MFR	rest	stress	MFR	rest	stress	MFR	rest	stress	MFR
0.75 ±0.24	3.10 ±1.15	4.28 ±1.44	0.73 ±0.22	3.05 ±1.23	4.30 ±1.46	0.80 ±0.28	3.82 ±1.79	5.05 ±2.38	0.72 ±0.25	2.68 ±0.83	3.81 ±0.98
0.64 ±0.09	2.80 ±0.88	4.38 ±1.40	0.64 ±0.08	2.82 ±0.85	4.46 ±1.30	0.68 ±0.11	3.44 ±1.55	5.15 ±2.40	0.62 ±0.08	2.37 ±0.63	3.86 ±0.99
0.98 ±0.33	3.75 ±1.48	4.07 ±1.67	0.93 ±0.29	3.54 ±1.86	3.97 ±1.90	1.05 ±0.38	4.66 ±2.18	4.84 ±2.60	0.96 ±0.33	3.36 ±0.85	3.71 ±1.08
p<0.01	NS	NS	p<0.01	NS	NS	p<0.01	NS	NS	p<0.01	p<0.05	NS

NS = non significant