



MYOCARDIAL PERFUSION IMAGING

Effects of Missing Dynamic Images on Myocardial Perfusion Reserve Index Calculation: Comparison Between an Every Heartbeat and an Alternate Heartbeat Acquisition[#]**Holger Thiele,^{1,*} Sven Plein,² John P. Ridgway,³ Marcel Breeuwer,⁴
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Philips Medical Systems, Best, The Netherlands**ABSTRACT**

A commonly used method for analysis of first pass myocardial perfusion imaging is the calculation of a myocardial perfusion reserve index (MPRI) obtained by dividing the upslopes of the time-intensity curves at stress and rest. Perfusion data can be acquired with several different sequences with images acquired at every single, 2nd, or 3rd heartbeat. During data acquisition, some images of the dynamic series can be missed due to extra beats. Twenty-six patients underwent first-pass magnetic resonance perfusion imaging, acquiring images every heartbeat at rest and stress. The maximal upslopes of the myocardium and the left ventricle were calculated for the original image series and for the image series from which dynamics of every 2nd heartbeat were removed. Additionally for each of these situations the upslope calculations were repeated but with the removal of one or two dynamics during the maximal upslope. Images acquired every 2nd heartbeat yielded a lower upslope for the myocardium and the left ventricle, but the resulting MPRI was unchanged. Removing dynamics during the upslope resulted in a change of the MPRI by up to 44% for every heartbeat acquisition and by up to 56% for an alternate sampling. In conclusion, missing data points may affect the calculation of MPRI values and should be taken into account when using such values to define a threshold, which discriminates between normally and abnormally perfused myocardium. Furthermore, it may lead to false positive or negative results in individual cases. This effect is increased if data are acquired only every 2nd heartbeat.

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INTRODUCTION

The presence and functional relevance of a coronary artery stenosis can be reliably detected by myocardial perfusion techniques, as there is a direct correlation between myocardial blood flow and myocardial oxygen supply. In routine clinical practice, perfusion assessment is most commonly performed with single photon emission computed tomography (SPECT). However, this method has a rather low spatial resolution with the inability to distinguish between subendocardial and transmural perfusion defects, exposes patients to ionizing radiation, and is hampered by attenuation artifacts (Hendel et al., 1999). Positron emission tomography corrects for attenuation and allows for the quantification of perfusion, but is burdened by a limited availability, high costs, and exposure to radiation (Muzik et al., 1998; Schwaiger, 1994).

Since its introduction in the early 1990s, myocardial first-pass magnetic resonance perfusion imaging has been used to detect coronary artery disease with similar sensitivity and specificity in comparison with SPECT imaging (Wilke et al., 1999). However, to date there is no consensus on the acquisition technique or the data analysis methods for myocardial perfusion imaging with MRI. In addition, several different qualitative, semiquantitative, and quantitative approaches have been used for image analysis. Recently, the most accurate results were shown to be obtained by a linear fit of the upslopes of the time-intensity curves of the myocardial signal and by the calculation of a myocardial perfusion reserve index (MPRI). This is derived by dividing the upslope value at stress by that at rest following correction for the left ventricular input function (Al-Saadi et al., 2000a,b). Thresholds have been defined to allow differentiation between normal myocardial segments and those with perfusion defects. However, as there are no standards for data acquisition, many different sequences have been used in these studies with acquisition either at every heartbeat, every 2nd, or every 3rd heartbeat and using multiple-slice or single-slice sequences (Al-Saadi et al., 2000a; Cullen et al., 1999; Schwitter et al., 2001; Slavin et al., 2001; Wilke et al., 1997). Differences in the temporal resolution (sampling rate) affect the number of points available for calculating the upslope of the resulting signal-intensity-time curves.

Furthermore, in particular under stress conditions dynamics can be missed due to ventricular or supraventricular extra systoles. This may have a more significant effect if data are acquired only every 2nd or 3rd heartbeat. The purpose of this study was to evaluate the effect of missing data points on the MPRI calculation and to compare this effect for a sampling rate at every heartbeat and every 2nd heartbeat. This was achieved by removing and processing selected images from a dynamic series acquired at every heartbeat.

METHODS

Study Population

Thirty-seven patients with suspected or known coronary artery disease underwent first-pass myocardial perfusion imaging after written informed consent. The study was approved by the local ethics committee. Patients were excluded from the study if they were hemodynamically unstable or had contraindications for MR examination (such as implanted pacemakers, metallic cerebral clips, etc.), reasons for inadequate image quality such as high-grade ventricular arrhythmias, atrial flutter or fibrillation, or contraindications to adenosine-infusion such as asthma or treatment with oral dipyridamole. Intake of any substances containing caffeine was stopped 12 hours prior to the MR study.

Magnetic Resonance Imaging

All patients were examined in the supine position with a whole body 1.5 Tesla MR system (Gyrosan Intera CV, Philips Medical Systems, Best, The Netherlands) equipped with Master gradients (30 mT/m peak gradients and 150 T/m/sec slew rate) and a 5-element cardiac phased-array coil for signal reception. A vectorcardiogram for electrocardiogram (ECG) gating and triggering was used (Chia et al., 2000). After two rapid surveys to define the orientation of the heart, four short-axis slices covering the heart from base to apex were acquired every heartbeat using an ECG-gated T1-weighted saturation recovery, segmented k-space gradient echo sequence

combined with a parallel acquisition method that uses sensitivity encoding (Pruessmann et al., 1999) (TR 3.1 ms, TE 1.6 ms, flip angle 15°, FOV 350–450 mm to avoid image aliasing, matrix 160 × 112, reconstructed to 256 × 256, 8 mm slice thickness, acquisition duration 115.8 ms/slice, SENSE-factor 2). Data were acquired over 40 seconds with 10 base-line dynamic images acquired during a first breath hold, followed by two respirations and a further breath hold. At the time of the 2nd respiration, a bolus of gadolinium-DTPA (Magnevist, Schering AG, Berlin, Germany) was rapidly injected by hand into an antecubital vein at a dose of 0.05 mmol/kg bodyweight followed by a flush of 10 ml saline. After 20–25 min, to allow for the clearance of the first bolus of contrast agent, adenosine at a dose of 140 µg/kg/min was administered for 5 min and image acquisition was repeated in the last 2 minutes of the infusion with the same geometry and acquisition parameters.

Image Analysis

Off-line image analysis was performed on a dedicated SPARC 10 Workstation (Sun Microsystems, Mountain View, CA) using prototype software (Easy-Scil, Medical Imaging Information Technologies, Philips Medical Systems, Best, The Netherlands). The endocardial and epicardial borders were drawn manually on each dynamic image. Additionally, a region of interest was drawn in the left ventricle with particular care to avoid the inclusion of myocardial segments and papillary muscles. The myocardium was divided into six equiangular segments and numbered clockwise beginning with the anterior septal insertion of the right ventricle; the segments were further subdivided into a subendocardial and subepicardial layer, resulting in 12 segments per slice (Fig. 1). The time-intensity profiles of the myocardium and the blood pool were transferred into an Excel-Worksheet (Excel 2000, Microsoft Redmond, WA, USA). The maximal upslopes of the total myocardium of each myocardial segment and of the left ventricular blood pool were calculated by a linear fit from the average time-signal intensity (SI) profiles using three points for the upslope calculation. Slice 2 was used for further analysis as being the most representative slice in the middle of the left ventricle with the most accurate time-intensity profiles without partial volume effects or left ventricular outflow tract in the imaging plane. To simulate acquisition in every 2nd heartbeat, the dynamic images of every 2nd heartbeat were removed from the original image series and maximum upslope values were

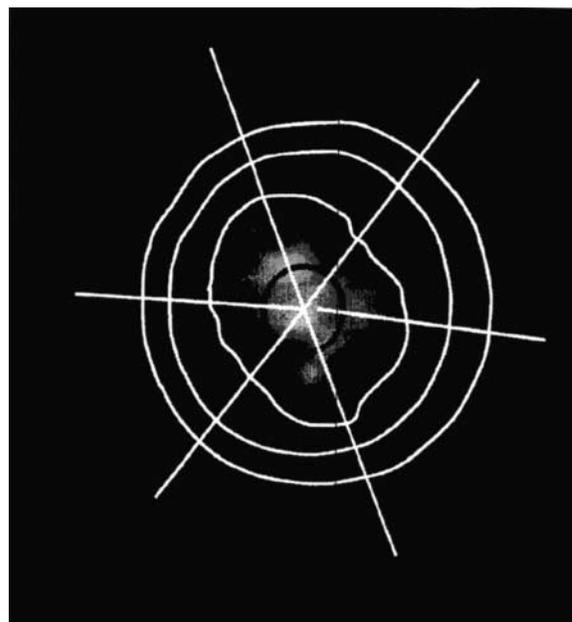


Figure 1. Short axis slice of the left ventricle, showing the 6 equiangular segments and division into a subendocardial and subepicardial layer.

recalculated (Fig. 2). Further, to simulate the occurrence of missing time points, upslopes were calculated after removing one or two images (Figs. 3, 4) during the maximal upslope (highest increase in the signal intensity over time) of the left ventricular blood pool and the myocardium for either at rest or stress or both. For each data set, the MPRI was calculated by dividing the results at stress by the results at rest for the myocardium as a whole and for all myocardial segments separately. Correction for the input function was performed, as defined previously (Al-Saadi et al., 2000a), resulting in the formula:

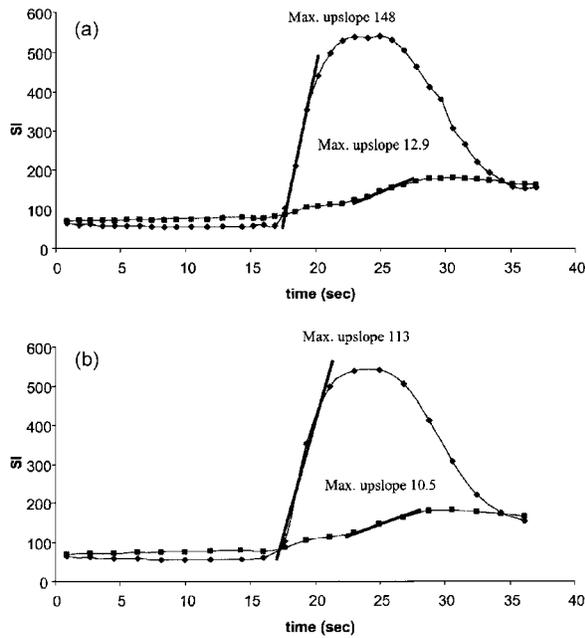
MPRI

$$= \frac{\text{upslope myocardium stress/upslope left ventricle stress}}{\text{upslope myocardium rest/upslope left ventricle rest}},$$

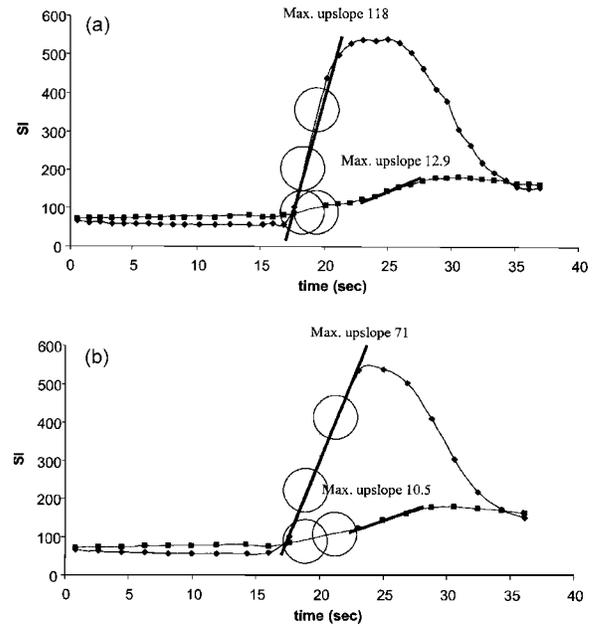
which was applied to all possible combinations of upslope calculation (Fig. 5).

Statistical Analysis

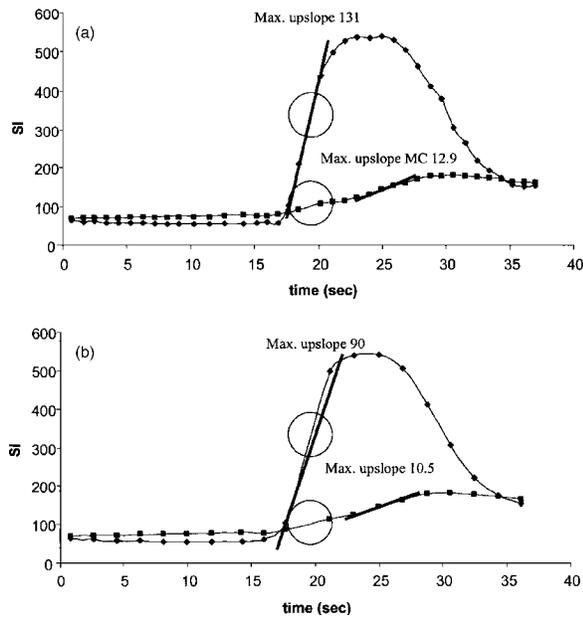
Each categorical factor is described as a number and a percentage. For continuous parameters the mean ± standard deviation is given. After testing of



Figures 2a and 2b. Patient example of the upslopes for the left ventricular blood pool and myocardium for every heartbeat and every 2nd heartbeat acquisition.



Figures 4a and 4b. Patient example of the upslopes for the left ventricular blood pool and myocardium for 2 missing dynamic images during the maximal upslope of the left ventricular blood pool at every heartbeat and every 2nd heartbeat acquisition (same patient as Fig. 2). Open circles indicate removed images.



Figures 3a and 3b. Patient example of the upslopes for the left ventricular blood pool and yocardium for 1 missing dynamic during the maximal upslope of the left ventricular blood pool at every heartbeat and every 2nd heartbeat acquisition (same patient as Fig. 2). Open circles indicate removed images.

the assumption that the differences are sampled from a Gaussian distribution by the method of Kolmogorov and Smirnov, results were compared by a paired *t*-test. Continuous parameters not sampled from a Gaussian distribution were compared by the nonparametric Wilcoxon rank sum test. The Chi-square test was used for categorical variables with nominal scales using statistical software (SigmaStat® 2.03, Version 2.0 SPSS Inc., San Rafael, CA, USA). All statistical tests

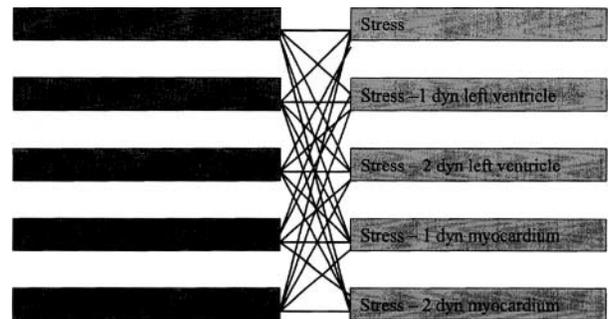


Figure 5. All possible combinations for MPRI calculation for image acquisition every or every 2nd heartbeat.

Table 1. Upslopes of the left ventricular blood pool, the whole left ventricular myocardium and resulting MPRI for each slice at image acquisition every heartbeat or every 2nd heartbeat.

| | Every heartbeat | Every 2 nd heartbeat | p value |
|-------------------|-----------------|---------------------------------|---------|
| Myocardium rest | 12.6 ± 6.5 | 10.2 ± 4.4 | <0.001 |
| LV rest | 126.3 ± 36.5 | 92.7 ± 26.5 | <0.001 |
| Myocardium stress | 16.8 ± 7.1 | 14.2 ± 5.6 | <0.001 |
| LV stress | 123.5 ± 58.6 | 91.2 ± 36.3 | <0.001 |
| MPRI | 1.6 ± 0.7 | 1.6 ± 0.7 | 0.95 |

LV = left ventricular blood pool; MPRI = myocardial perfusion reserve index.

were two-tailed and a p value <0.05 was considered statistically significant.

RESULTS

Due to technical problems (n = 3, 8%) and due to missed dynamics on the original data set during the acquisition at rest or stress (n = 8, 22%) 11 patients (30%) had to be excluded, thus resulting in a study population of 26 patients. Mean age was 62 ± 9 years (range 43–79); 14 patients were male and 12 female. In all 26 patients images obtained were appropriate for tracing of the endo- and epicardial contours and for generation of time-intensity profiles of the left ventricular blood pool and the myocardium. All patients tolerated the imaging procedure, the contrast agent, and adenosine administration well.

Upslope calculation for a sampling rate at every 2nd heartbeat yielded lower upslope values for

the myocardium and the left ventricular blood pool in comparison to those obtained using the full data set (Table 1 and Fig. 2a,b). There was no difference in the resulting MPRI between the two sampling rates (1.6 ± 0.7 vs. 1.6 ± 0.7, p = n.s.). Highly significant differences for MPRI values were obtained when images were removed from the maximum upslope period of the data obtained at every heartbeat. Even greater differences resulted when images were removed from the alternately sampled image datasets (Table 2, Fig. 3a,b, Fig. 4a,b).

According to the formula previously defined, for all four situations (during rest and stress, with missing images and without) the calculated MPRI of missing images during stress or rest had a range from 1.1 ± 0.4 to 2.3 ± 1.0 for a sampling rate at every heartbeat, and a range from 0.8 ± 0.3 to 2.5 ± 1.1 for a sampling rate at every 2nd heartbeat (Table 3a,b). There were differences of up to 44% for data acquired every heartbeat and up to 56% for data acquired with alternate sampling, respectively.

Table 2. Effects of missing dynamic images on upslopes in every heartbeat and every 2nd heartbeat acquisition.

| | MC rest | LV rest | MC stress | LV stress |
|---------------------------------|-------------------------|---------------------------|-------------------------|---------------------------|
| Every heartbeat | 12.6 ± 6.5 | 126.3 ± 36.5 | 16.8 ± 7.1 | 123.5 ± 58.6 |
| 1 dynamic missed LV | 12.6 ± 6.5 | 111.1 ± 31.1 ^a | 16.7 ± 7.2 | 108.8 ± 47.7 ^a |
| 2 dynamics missed LV | 12.5 ± 6.5 | 97.5 ± 27.7 ^a | 16.7 ± 7.2 | 97.0 ± 42.4 ^a |
| 1 dynamic missed MC | 11.8 ± 6.6 ^a | 126.3 ± 36.5 | 15.4 ± 6.3 ^a | 123.1 ± 59.0 |
| 2 dynamics missed MC | 11.4 ± 6.5 ^a | 125.1 ± 36.7 | 14.4 ± 6.0 ^a | 123.0 ± 59.2 |
| Every 2 nd heartbeat | 10.2 ± 4.4 | 92.7 ± 26.5 | 14.2 ± 5.6 | 91.2 ± 36.3 |
| 1 dynamic missed LV | 10.0 ± 4.4 | 71.0 ± 19.8 ^a | 13.4 ± 5.5 ^b | 74.6 ± 29.4 ^a |
| 2 dynamics missed LV | 9.8 ± 4.4 | 56.0 ± 16.2 ^a | 12.6 ± 5.6 ^a | 60.1 ± 24.2 ^a |
| 1 dynamic missed MC | 9.0 ± 3.4 ^a | 89.9 ± 27.5 | 12.6 ± 4.9 ^a | 90.2 ± 36.0 |
| 2 dynamics missed MC | 8.2 ± 3.1 ^a | 89.3 ± 28.1 | 11.4 ± 4.6 ^a | 89.1 ± 36.9 |

MC = myocardium; LV = left ventricular blood pool.

^ap < 0.001 vs. no missing dynamic for every heartbeat or every 2nd heartbeat acquisition at rest or stress.

^bp < 0.05 vs. no missing dynamic for every heartbeat or every 2nd heartbeat acquisition at rest or stress.

Table 3a. MPRI calculation after the removal of different combinations of missing dynamic images from an every heartbeat acquisition.

| MPRI | Stress | Stress - 1 dyn. LV | Stress - 2 dyn. LV | Stress - 1 dyn. MC | Stress - 2 dyn. MC |
|------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Rest | 1.6 ± 0.7 | 1.8 ± 0.8 ^a | 2.0 ± 0.9 ^a | 1.5 ± 0.7 ^a | 1.4 ± 0.6 ^a |
| Rest - 1 dyn. LV | 1.4 ± 0.6 ^a | 1.6 ± 0.7 | 1.8 ± 0.8 ^a | 1.3 ± 0.6 ^a | 1.2 ± 0.5 ^a |
| Rest - 2 dyn. LV | 1.3 ± 0.5 ^a | 1.4 ± 0.6 ^a | 1.5 ± 0.6 | 1.1 ± 0.5 ^a | 1.1 ± 0.4 ^a |
| Rest - 1 dyn. MC | 1.7 ± 0.8 ^a | 1.9 ± 0.8 ^a | 2.2 ± 0.9 ^a | 1.6 ± 0.7 | 1.5 ± 0.6 ^b |
| Rest - 2 dyn. MC | 1.8 ± 0.8 ^a | 2.0 ± 0.9 ^a | 2.3 ± 1.0 ^a | 1.7 ± 0.7 | 1.6 ± 0.7 |

MPRI = myocardial perfusion reserve index.

dyn. = dynamic image.

LV = left ventricular blood pool.

MC = myocardium.

^ap < 0.001 vs. MPRI without missing dynamics.^bp < 0.05 vs. MPRI without missing dynamics.

Applying an arbitrary empirically defined threshold for the MPRI of 1.2, 101 of all 312 (32%) segments had an abnormal perfusion based on the MPRI calculated using time points for every heartbeat compared with 113 segments (36%) when using MPRI values calculated using time points from alternate beats. The removal of images during the upslope of the left ventricular blood pool or myocardial tissue led to a different classification to “normal” or “abnormal” compared with the original analysis of up to 65 segments (57%) at a sampling rate of every 2nd heartbeat (Table 4).

DISCUSSION

In patients with coronary artery disease myocardial blood flow and flow reserve are inversely but nonlinearly

related to the severity of stenosis as defined by quantitative coronary angiography (DiCarli et al., 1995; Gould et al., 1974; Uren et al., 1994). The challenge for perfusion imaging is to estimate the functional significance of a coronary artery stenosis. First-pass MR perfusion provides a relatively new noninvasive technique, but currently there is no consensus on the optimal MR sequence and the method of data analysis. Since its introduction in the early 1990s the results have been first assessed qualitatively with further steps directed at a semi- or quantitative analysis (Hartnell et al., 1994; Klein et al., 1993; Walsh et al., 1995). The quantification of myocardial perfusion is usually performed in two steps: 1) obtain a concentration time curve from a signal-intensity time curve; 2) extraction of parameters of myocardial perfusion from the concentration time curve. The most widely used concept of

Table 3b. MPRI calculation after removal of different combinations of missing dynamic images from an alternate heartbeat acquisition.

| MPRI | Stress | Stress - 1 dyn. LV | Stress - 2 dyn. LV | Stress - 1 dyn. MC | Stress - 2 dyn. MC |
|------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Rest | 1.6 ± 0.7 | 1.8 ± 0.7 ^a | 2.1 ± 0.8 ^a | 1.4 ± 0.6 ^a | 1.3 ± 0.5 ^a |
| Rest - 1 dyn. LV | 1.3 ± 0.5 ^a | 1.4 ± 0.5 ^b | 1.7 ± 0.6 | 1.1 ± 0.4 ^a | 1.0 ± 0.4 ^a |
| Rest - 2 dyn. LV | 1.0 ± 0.4 ^a | 1.1 ± 0.4 ^a | 1.3 ± 0.5 ^b | 0.9 ± 0.3 ^a | 0.8 ± 0.3 ^a |
| Rest - 1 dyn. MC | 1.7 ± 0.8 ^b | 2.0 ± 0.7 ^a | 2.3 ± 0.9 ^a | 1.6 ± 0.6 | 1.4 ± 0.6 ^c |
| Rest - 2 dyn. MC | 1.9 ± 0.9 ^a | 2.2 ± 0.9 ^a | 2.5 ± 1.1 ^a | 1.7 ± 0.8 | 1.6 ± 0.6 |

MPRI = myocardial perfusion reserve index.

dyn. = dynamic image.

LV = left ventricular blood pool.

MC = myocardium.

^ap < 0.001 vs. MPRI without missing dynamics.^bp < 0.005 vs. MPRI without missing dynamics.^cp < 0.05 vs. MPRI without missing dynamics.

Table 4. Number (%) of all 312 segments classified as abnormal perfusion at an MPRI threshold of 1.2 for different combinations of missing dynamic images removed from every heartbeat or every 2nd heartbeat acquisitions.

| | No. missing dynamic | – 1 dyn. LV | – 2 dyn. LV | – 1 dyn. MC | – 2 dyn. MC |
|---|---------------------|-------------|------------------------|-------------|-------------|
| Every heartbeat acquisition | 101 (32%) | 107 (34%) | 113 (36%) | 103 (33%) | 99 (31%) |
| Every 2 nd heartbeat acquisition | 113 (36%) | 136 (44%) | 178 (57%) ^a | 121 (39%) | 129 (41%) |

MPRI = myocardial perfusion reserve index.

dyn. = dynamic image.

LV = left ventricular blood pool.

MC = myocardium.

^a $p < 0.001$ vs. MPRI without missing dynamics.

quantitative perfusion analysis has been derived from the indicator-hemodilution theory (Meier and Zierler, 1954), which is based on several necessary requirements: 1) complete mixing of the indicator proximal to the sampling site; 2) the intravascular contrast agent used should have no extravascular loss during the firstpass; 3) stable hemodynamics during data acquisition; 4) complete washout of the contrast agent; 5) an instantaneous Dirac delta input function without recirculation and; 6) a linear correlation between tracer and signal intensity. However, for MR perfusion imaging and measurement these criteria are not fulfilled with the gadolinium-chelates currently in routine use. These distribute into the extracellular space rapidly and the linearity between contrast agent and signal intensity is only maintained at low concentrations of less than 1.3 to 2.0 mmol/l (Canet et al., 1995; Koenig et al., 1986). Furthermore, the injection of the contrast agent into a peripheral vein may lead to a dispersion of the contrast bolus. Therefore, extensive modeling and assumptions regarding water exchange or contrast agent distribution and mean transit time of the contrast agent are required for a quantitative analysis. Such models have been used and validated by several groups in animals and small numbers of patients, but are considered to be too sophisticated for clinical purposes (Diesbourg et al., 1992; Fritz-Hansen et al., 1998; Jerosch-Herold and Wilke, 1997; Jerosch-Herold et al., 1998; Larsson et al., 1996; Vallée et al., 1997; Vallée et al., 1999; Wilke et al., 1993; Wilke et al., 1997). To circumvent these problems associated with quantitative analysis, semi-quantitative parameters of the time-intensity curve, such as the upslope, the time to peak signal intensity and the peak signal intensity have been used (Al-Saadi et al., 2000a,b; Eichenberger et al., 1994; Matheijssen et al., 1996; Schaefer et al., 1992; Schwitter et al., 2001; Walsh et al., 1995). For extravascular contrast agents, the early part of

the time-intensity curve is mainly influenced by perfusion, and the later parts are increasingly influenced by diffusion. Therefore, measurements of the maximal upslope during the first pass of extravascular contrast agents provide a reasonable estimate of myocardial perfusion. The application of a linear fit of the maximum time-intensity curve upslopes and the calculation of a MPRI after rest and stress perfusion has been shown to be highly accurate and reproducible in terms of inter- and intraobserver variability for the detection of significant coronary artery disease after the definition of a threshold (Al-Saadi et al., 2000a,b). Another approach using only the upslopes during stress revealed similar sensitivities and specificities (Schwitter et al., 2001).

MR Sequences Used for Myocardial Perfusion

There are several requirements for MR perfusion imaging: 1) the coverage of most of the left ventricle by multiple slices; 2) a high temporal resolution to allow assessment of the first pass of the contrast agent; 3) a good dynamic range of contrast; and 4) a high spatial resolution to discriminate between normal regions and perfusion deficits. A variety of different sequences with saturation or inversion pulses, with acquisition every single, 2nd, or even 3rd heartbeat and with a different number of slices have been used so far to meet these requirements, but usually have made compromises due to hardware and software constraints (Al-Saadi et al., 2000a; Ding et al., 1998; Fischer et al., 1996; Schwitter et al., 1997; Slavin et al., 2001; Keijer et al., 2000; Wilke et al., 1997). The results from this study underline the importance of acquiring data with a high temporal resolution, as the effects of missing data are more pronounced at a lower sampling rate.

Prevalence of Missing Dynamics During Myocardial Perfusion

This study demonstrates that missing dynamic images during the first pass of the contrast agent is a frequent phenomenon in myocardial perfusion imaging. Despite using a state-of-the-art vectorcardiographic method for ECG-triggering and care taken to acquire a stable ECG signal prior to imaging, eight of 37 patients (= 22%) showed missing images either during rest or stress acquisition and were thus excluded from further study. When the effect of missing images was simulated by removing data points during the maximum upslopes, the resulting MPRI changed by up to 44% for analysis of data from every heartbeat and by as much as 56% for analysis of data from every 2nd heartbeat. An assessment of the frequency of missing images during the upslope period and the effect on its calculation has not been reported in previous studies. However, in one study 7.5% of the patients had to be excluded due to insufficient ECG triggering because of frequent premature ventricular complexes (Al-Saadi et al., 2000a). As we have used a perfusion and stress model similar to that of other groups, recommended by a consensus panel report (Nagel et al., 2001), the percentage of missing dynamic images during the upslope of either the myocardium or the left ventricular blood pool should be considered representative. In this study, adenosine was used as a stress agent, while other investigators have used dobutamine for stress perfusion imaging, which is known to have even more arrhythmogenic effects than adenosine or dipyridamol (Wahl et al., 2001).

Correction for Left Ventricular Input Function

One factor influencing the resulting MPRI is the additional division by the upslope of the left ventricular input function during rest and stress, which leads to the propagation of errors in the MPRI calculation. The correction for the left ventricular input function is mandatory for a quantitative assessment of myocardial perfusion according to the indicator-hemodilution theory (Meier and Zierler, 1954). However, for semiquantitative assessment using an MPRI, a correction for the left ventricular input is also commonly accepted because the hemodynamic characteristics are different during rest and stress and the characteristics of the contrast bolus can differ especially when manual contrast injections are used (Al-Saadi et al., 2000a; Eichenberger et al., 1994; Schwitzer et al., 2001).

Study Limitations

One limitation of this study is the fact that a manual injection was performed, which can lead to greater variability of the input function when compared to injection with an automatic power injector. However, the correction for the left ventricular input function should eliminate differences in infusion speed of the contrast agent, thus making this limitation negligible. Furthermore, the acquisition of images for every alternate heartbeat and the presence of missing images in this study was simulated by removing data points from the full data sets of every heartbeat acquisition. Thus, the presented results suffer from the inherent difference between real and simulated data. Nevertheless, in reality other factors contribute to differences between every heartbeat and every 2nd heartbeat acquisition like patient movement or breathing, thus influencing the real results more unfavorably. Finally, the threshold used in this study was arbitrarily defined. This is in contrast to other studies, in which cut-off values were defined from normal volunteers and patients with single vessel disease. For our study, an exactly defined threshold would have been of little relevance because we carried out computer simulations of the effects of missing dynamics on the MPRI and the number of segments above and below a threshold. The results would therefore have been very similar with any other threshold. In a recent study with peripheral venous injection the mean MPRI was in the range of 1.4 ± 0.5 for stenosis between 50–75% and 1.2 ± 0.3 for stenosis > 75% (Ibrahim et al., 2002). Applying formerly used methods to define a cut-off value (cut-off point 2 standard deviations below the mean MPRI of normals) would have resulted in a value even below 1.2. Therefore we chose a threshold, which was in the range of those previously defined (Al-Saadi et al., 2000a; Ibrahim et al., 2002).

CONCLUSION

Missing data points may affect the calculation of MPRI values and should be taken into account when using such values to define a threshold that discriminates between normally and abnormally perfused myocardium. Furthermore, it may lead to false positive or negative results in individual cases. This effect is increased if data is acquired only every 2nd heartbeat. Sequences that acquire data every heartbeat should be recommended. However, they should still be carefully checked for missing dynamic images during the upslope of the time-intensity curve. In cases where data points are



missing for the upslope calculation, the results should be interpreted with caution.

ABBREVIATIONS

Dyn. = dynamic image
ECG = electrocardiogram
LV = left ventricular blood pool
MC = myocardium
MPRI = myocardial perfusion reserve index
MR = magnetic resonance
SI = signal intensity
SPECT = single photon emission computed tomography

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