

# DOBUTAMINE AS AN APPROPRIATE AGENT FOR DETECTING MECHANICAL HEART PROPERTIES AND DIFFERENT COMPONENTS WITHIN THE IMPEDANCE CARDIOGRAM

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**Abstract:** The effects of sympathetic stimulation by Dobutamine were investigated in order to expand our knowledge of the mechanical heart action and to improve the understanding of Impedance Cardiography (ICG). US Doppler and ICG signals were recorded at baseline without Dobutamine, after application of 5g ( $g = \mu g \cdot kg^{-1} \cdot min^{-1}$ ) and subsequently of 10g Dobutamine in 20 healthy male subjects. As a result we found a highly reproducible double peak in the C-wave of the ICG, which is dependent on the concentration of Dobutamine and the respiration cycle. We therefore conclude, that Dobutamine may be an appropriate agent for detecting different physiological components within the ICG and may also reveal important information about the mechanical properties of the heart, like contractility.

**Keywords:** Impedance Cardiography, Dobutamine, Sympathetic Stimulation, Systolic Time Intervals

## Introduction

It is a well-known fact that the ICG reflects different physiological phenomena, like aortic and pulmonary flow, blood volume changes in the aorta and the pulmonary artery, respiration and movement of the aorta [1,2]. However, under normal conditions these phenomena cannot be identified from the ICG. During measurements with our newly developed physiological measurement device (PMD) on 20 healthy male subjects we found a highly reproducible, respiratory dependent double peak in the ICG under the application of Dobutamine (fig. 1), a  $\beta_1$ -adrenoreceptor agonist, which stimulates cardiac inotropy. The objective of this study was to examine, whether these characteristic double peaks allow us to identify different important physiological components within the ICG.

## Materials and Methods

In each examination, all signals including US and ICG were recorded at baseline without Dobutamine, after application of 5g and subsequently of 10g Dobutamine. The interval between the injections and the recording of data was about 10min, long enough for the physiological system to reach a steady state.

For the evaluation of a double peak intensity we divided the appearance of double peaks into 8 different classes, dependent on the difference between their am-

plitudes and the gap between both peaks. From all intensities of the different subjects the respective intensity found in their baseline data was subtracted in order to make them comparable among each other, since some subjects had double peaks even without Dobutamine.

We also divided the respiration cycle, which was reconstructed from  $\Delta Z$ , into 8 different intervals, 1 to 4 for expiration and 5 to 8 for inspiration. That allowed us to plot the measured mean values and standard deviations of the determined double peak intensities as a function of the respiration cycle (fig. 2). Representing the inspiration and expiration intervals as a single continuous function and normalizing this function to  $\pm 1$  allowed us to calculate the normalized cross correlation function between the respiration cycle and the intensity of the double peaks.

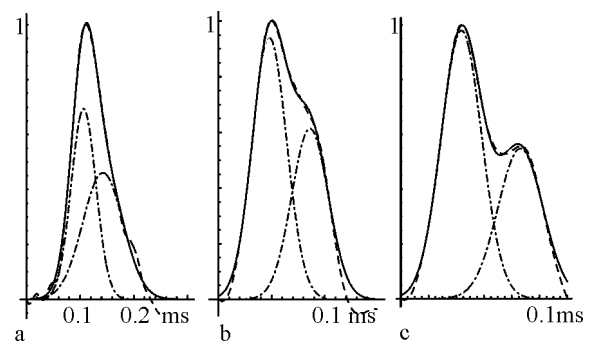


Figure 1: Typical C-waves. Time zero coincides with the R-peak of the ECG. Dashed line: measured signal, solid line: C-waves approximated by two Gaussian functions (dot-dashed lines). a: no Dobutamine, no double peak; b: Inspiration, 10g Dobutamine, weak double peak; c: Expiration, 10g Dobutamine, pronounced double peak.

In order to demonstrate that the double peaks can reliably and precisely be reconstructed on the basis of two components, we approximated for each respiration class and each Dobutamine concentration the C-wave as a superposition of two Gaussian functions (fig. 1). The mean values in these functions stand for the times at which these components have their highest contribution to the C-wave, and the standard deviation and the amplitudes represent the width and the highest intensity of these components. In order to determine the Gaussian parameters we used the least squared error method.

## Results

We found a highly reproducible appearance of double peaks after the application of Dobutamine, which were more pronounced during expiration than inspiration. Fig. 2 shows the averaged double peak intensities from one subject as a function of Dobutamine concentration and respiration. The correlation coefficients were about 0.72 for the high and 0.53 for the low Dobutamine concentration, both found in the cross correlation functions at a mean time shift of 0.

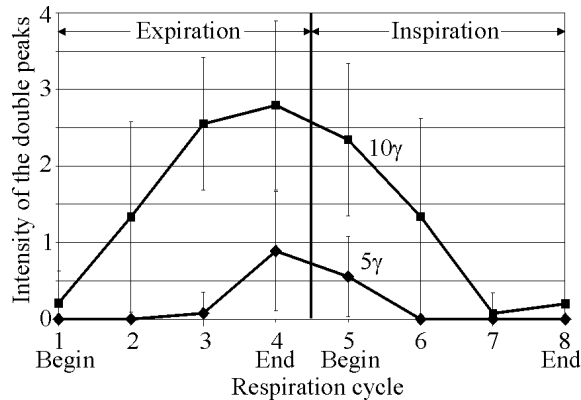


Figure 2: Mean values and standard deviations of the respiration and concentration dependent double peak intensities.

Our approximations of the C-wave by two Gaussian functions showed a reproducible shift of their mean values, i.e. their highest amplitudes towards shorter pre-ejection periods (PEPs), the higher the Dobutamine concentration the higher the shift. This was expected as  $\hat{\alpha}$ -adrenergic stimulation is known to shorten PEPs by increasing inotropy [3]. Due to our preliminary data analyses, the time shifts in both components are not the same neither in the different respiration classes at constant Dobutamine concentration nor at different Dobutamine concentrations within the same respiration class. There are strong indications that both components are differently influenced by the respiration cycle and Dobutamine concentrations since the other Gaussian parameters show also dissimilar dependencies on these variables.

With high concentrations of Dobutamine we interestingly found that the aortic valve opened before the depolarization of the heart was complete. The opening of the aortic valve coincided with the onset of the first heart sound. The pre-ejection period was only about 40ms, surprisingly short compared to about 100ms without Dobutamine. The surprisingly strong shortening of the PEP was confirmed by data from the US Doppler device.

## Discussion

The influence of Dobutamine on the ICG and the decomposition of the C-wave into different components

were already investigated in earlier studies [4]. These studies, however, did not reveal any systematical repeatability of double peaks, nor did they provide data that allowed to establish a valid link between the different components of the ICG and a related physiological event. We assume that the different outcome of our study may be due to the augmented quality of our ICG measurements, which has been achieved due to our new ICG recorder, and for the first time, provides reproducible and precise data, which reliably shows that under the influence of Dobutamine there are reproducible changes in the haemodynamics of the cardiovascular system. These allowed us to reliably and reproducibly determine parameters of the different components, such as the time shifts of their peaks. Until now, however, the interpretation of these parameters which may reveal further important information about the origin of the ICG and the mechanical properties of the heart, are still under investigation.

According to our findings the interpretation of the first heart sound must be reviewed. The generally accepted interpretation of the phonocardiogram is based on the assumption that the onset of the first sound reflects the beginning of the isovolumetric contraction period which occurs well before the aortic valve opens, indicated by an incision in the sound. This does not hold for our subjects after Dobutamine infusion, where the valve already opens almost simultaneously with the onset of the first heart sound, which was confirmed by data from the US device.

## Conclusions

From our findings we conclude that Dobutamine is an appropriate agent for the detection of physiological components within the ICG, which is mainly due to the highly reproducible appearance of respiratory dependent double peaks during sympathetic stimulation. Identifying the origins of these components will lead to additional important noninvasively assessable information about the cardiovascular system.

## REFERENCES

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