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# The role of microwave radiometry in carotid artery disease. Diagnostic and clinical prospective

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Atherosclerosis of the internal carotid artery is an important cause of disabling ischemic stroke and therefore constitutes a major medical, social, and economic issue. Although advances in vascular imaging modalities during the last decades allow to risk stratify patients not solely on the degree of carotid artery stenosis but also based on 'high risk' features, there still remains a controversy over patient selection for carotid artery revascularization. Among other features of plaque vulnerability, there is an increasing body of evidence that inflammation is a key factor in the initiation, progression and destabilization of atherosclerotic plaques. Microwave radiometry (MWR) is a new imaging method that is based on the ability to detect noninvasively, with high accuracy, the relative changes of temperature in human tissues reflecting inflammatory activation. This review article aims to: (1) give an overview of current clinical experience with MWR in carotid arteries and (2) present its potential role for risk stratification.

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## Background

Atherosclerosis of the internal carotid artery is an important cause of disabling ischemic stroke and therefore constitutes a major medical, social, and economic issue [1]. During the last decades, advances in imaging modalities have changed the landscape of carotid artery disease management; however, there still remains a controversy over patient selection for carotid artery revascularization [2–5].

According to the recently published European Society of Cardiology (ESC) Practice Guidelines on peripheral arterial disease, the grade of stenosis and the presence of symptoms are the main grounds to decide for carotid revascularization [1]. Symptomatic patients with significant carotid artery stenosis (>50%) should always be considered for revascularization in addition to best medical therapy. The management however, of asymptomatic carotid artery disease — despite the improved prognosis with best medical therapy — remains controversial. Based on current guidelines and pending the development of better algorithms, asymptomatic patients with moderate or severe stenosis (60–99%) having clinical and/or imaging features associated with increased risk for stroke ('high risk features') may also be considered for revascularization [1].

Although recent advances in vascular imaging modalities allow to risk stratify asymptomatic patients not solely on the degree of carotid artery stenosis but also based on how vulnerable the plaque is to rupture, risk stratification remains challenging [2]. Actually, there is an emerging interest in medical science to find imaging strategies that allow identification of patients who are at the highest risk of cerebrovascular complications [3–5].

Among features of vulnerability, there is an increasing body of evidence that inflammation is a key factor in the initiation, progression and destabilization of atherosclerotic plaques [6]. Microwave radiometry (MWR) is a new imaging method that is based on the ability to detect noninvasively, with high accuracy, the relative changes of temperature in human tissues reflecting inflammatory activation. This review article aims to: (1) give an overview of current clinical experience with MWR in carotid arteries and (2) present its potential role for risk stratification.

## Carotid artery plaque features: the concept of plaque vulnerability and inflammation

Research has shown that the biological properties of the carotid plaque itself are important for its stability and that inflammation plays an important pathogenic role in all stages of plaque development, including rupture. Histological features associated with plaque instability are the presence of thin fibroatheromatous cap that overlies a large lipid pool (>40% of the plaque), large necrotic core, intimal spotty calcification, high inflammatory cell concentration, neovascularization and intraplaque hemorrhage [7]. The terms vulnerable, unstable or 'high-risk' are now widely used to describe plaques that exhibit such features. Although these features were initially identified histologically, advances in imaging techniques have made their *in vivo* identification possible.

## Thermography

The concept that local inflammation can be detected by local heat production was originally proposed on the basis of observations from human *ex vivo* carotid endarterectomy specimens [8]. In 1996, Casscells *et al.* measured the intimal surface temperatures of 20 sites at 50 samples of carotid plaques taken during surgical endarterectomy, using a sensitive needle thermistor [8]. The measurement revealed several regions in which the surface temperatures varied from 0.2 to 0.3 °C, but 37% of plaques had points not distinguished by naked eye, with substantially different temperatures (0.4–2.2 °C). These results were reproducible, while thermal heterogeneity ($\Delta T$) could also be confirmed using an infrared camera *in vivo*. Furthermore, plaque temperature was directly correlated with inflammatory cell density ($R = 0.68$, $p = 0.0001$) and inversely to the distance of the cell clusters from the luminal surface ($R = -0.38$, $p = 0.0061$).

This *ex vivo* study that demonstrated for the first time that localized heat is generated from inflamed atherosclerotic plaques in humans was followed by *in vivo* clinical studies and the introduction of intravascular thermography that confirmed the aforementioned findings [8–15]. Intravascular thermography provided additional diagnostic and prognostic information in the identification of the high risk atheromatic plaques in patients with coronary artery disease (CAD); however, its invasive character excluded this method from primary prevention.

## Principles of microwave radiometry

Microwave radiometry was first introduced in cardiology in 2012 as a simple non-invasive method for the identification of vascular inflammatory activation with similar accuracy and as an alternative method to intravascular thermography [16]. The system provides accurate assessment of local inflammatory activation by measuring temperature from internal tissues at microwave frequencies.

Measurements are performed by a microwave computer-based system (RTM-01-RES, Bolton, United Kingdom) and are based on the principle that the intensity of the radiation is proportional to the temperature of tissue [16,17]. It possesses an antenna with two sensors: a microwave and an infrared. The microwave sensor detects microwave radiation from the 'volume under investigation' that is a rectangular area of 3 cm in width, 2 cm in length, and 3–7 cm in depth depending on the dielectric properties of the underlying tissues, the wavelength, and the water content of the tissue. The infrared sensor is used for infrared measurements from the skin, for calibrating the microwave sensor readings. The detailed technical characteristics of the MWR system are presented in Table 1.

## Application of MWR in vascular medicine

### In an experimental model

Microwave radiometry was validated with the gold standard method for the assessment of thermal heterogeneity that is intravascular thermography [18]. In this study 24 New Zealand White rabbits were randomly assigned to a normal diet, whereas 12 others were fed a cholesterol-rich diet (0.3% cholesterol and 4.7% coconut oil) for 6 months. Thereafter all rabbits were prepared for intravascular angiography, intravascular thermography and MWR of the abdominal aorta. In order to ensure that temperature measurements were performed at the same segments with the two different methods, the abdominal aortas were divided by optical coherence tomography (OCT) in five consequent segments of equal length (2 cm) and external radiopaque markers were placed in between. Temperature measurements obtained with MWR were similar to measurements obtained by intravascular thermography. Moreover, temperature differences of hypercholesterolemic segments assessed by both methods correlated with plaque thickness and inflammatory infiltrates assessed by histology. This study showed for the first time that MWR is a safe and feasible method

**Table 1**

**The technical specifications of the RTM-01-RES.**

| Items | Specifications |
|---|---|
| Depth of detection of a thermal abnormality (higher or lower temperature), cm | 3–7 (depending on water content) |
| Width of detection of a thermal abnormality, cm | 2 |
| Accuracy of measuring the internal temperature, when the temperature range is 32–38 °C | ±0.2 °C |
| Time of measuring internal temperature at one point, seconds | 8 |
| Applicator diameter, mm | 39 |
| Accuracy of skin temperature measurement, °C | ±0.2 |
| Time of measuring skin temperature at one point, second, when the temperature range is 32–38 °C, seconds | 1 |
| System weight, kg | 4 |
| Power supply | 220 ± 22 Volt 1 phase, 50 Hz |

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