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# *Chapter VII*

## Molecular imaging of ischemia and angiogenesis – Introduction

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The term "molecular imaging" is broadly defined as the *in vivo* characterization and measurement of biological processes on the molecular level. Whereas the "classical" diagnostic imaging techniques show the outcome of biochemical abnormalities, molecular imaging characterizes molecular alterations and identifies molecular pathways of diseases. The development of approaches combining radiological and molecular biological imaging technologies is ideal for a complex evaluation of pathologic events in the human organism. This combination opens a new window for diagnostics and therapy.

Since a few years the new scientific field "molecular radiology" is developing focusing particularly on cardiovascular and oncologic diseases which are the most spread courses of human death. Although for contradictional applications, an "angiogenesis" is the common research field for both cardiovascular (improvement of perfusion) and oncologic (suppression of tumor vascularization) points of view: Up-regulation or down-regulation of the angiogenic process is central to approximately 30 actually studied cardiovascular, oncologic and immunologic diseases including *diabetes mellitus*.

Cellular and molecular information about the *in vivo* state can be obtained with improved imaging technologies like high resolution MR, $\mu$PET, etc. One of the most important parameters is the information about the spread of apoptosis in a tissue. Imaging of the accumulation of apoptotic molecular markers like caspase-3 and annexin V localizes the apoptotic areas *in vivo*. The kinetics of DNA damage and fragmentation *ex vivo* using for example the method of "comet assay" analysis open a possibility to distinguish among apopototic and necrotic cell death as well as DNA repair deficiencies.

The new molecular biological approach "gene hunting" using complex DNA, mRNA, and protein assays is able to analyse a differential gene expression *ex vivo* and is applicable to all types of tissues. This is the key-approach to identify molecular alterations in complete pathways consequently coursing a particular disease of interest. On the basis of this information the most suitable therapy forms could be chosen. The effect of therapeutic agents could be observed *in vivo* using MR-Imaging and *ex vivo* using specific assays on the molecular level.

Ischemia developed due to perfusion disturbances may play a major role in initiation of secondary diseases like glaucoma. The role of leukocytes as inflammatory mediators of secondary injury after ischemic events has been recognized in the brain as well as other body organs. *In vivo* evidence of adherent leukocytes induced by global cerebral ischemia has been provided early after brain damage. Activated leukocytes may impair blood flow by disturbing microcirculation, exacerbate endothelial cell injury by releasing hydrolytic enzymes or by producing oxygen free radicals, and migrate into the ischemic parenchyma to interact with neurons and other supportive cells. Recent studies of the differential gene expression in circulating leukocytes of vasospastic patients show the existence of potential molecular markers in blood leukocytes which could be used for early noninvasive diagnostics of different forms of an angiopathy and a vasospastic syndrome.

Molecular imaging of ischemia and angiogenesis provides insights into mechanisms of disease initiation, allows early noninvasive diagnostics, and the development of preventive treatments.