A new water-specific technique for local measurement of edema and lymphedema induced by cancer therapy*

Tapani Lahtinen¹, Jouni Nuutinen² and Harvey N. Mayrovitz³
¹Department of Oncology, Kuopio University Hospital; ²Delfin Technologies Ltd, Kuopio, Finland; ³Department of Physiology, Nova Southeastern University, Ft. Lauderdale, USA

Edema can be defined as soft tissue swelling due to expansion of the interstitial volume. In cancer therapy edema can be localized (following surgery or radiotherapy RT) or generalized (following use of drugs). Combined use of RT, surgery or drugs may cause secondary lymphedema, for instance, in a patient's arm after radical mastectomy. Unfortunately, there have not been objective water-specific tools that help with accurate diagnosis of edema or lymphedema. The early detection and effective management of edema can have many potential benefits (Table):

<table>
<thead>
<tr>
<th>Table: Potential benefits of early edema detection and management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Reduced tissue swelling</td>
</tr>
<tr>
<td>2. Reduced edema-related pain</td>
</tr>
<tr>
<td>3. Improved mobility of the extremities</td>
</tr>
<tr>
<td>4. Reduced misfigurement</td>
</tr>
<tr>
<td>5. Reduced fibrosis</td>
</tr>
<tr>
<td>6. Greater limb function</td>
</tr>
<tr>
<td>7. Improved quality of life</td>
</tr>
<tr>
<td>8. Increased understanding of underlying processes</td>
</tr>
</tbody>
</table>

Previous techniques to assess edema

Previous techniques to assess edema include compression techniques, skin-fold measurements, water displacement techniques, circumference measurement, perometry, bioelectrical impedance, ultrasound and MR imaging. Due to its water-specificity the latter is evidently the best available method for the evaluation of deep or superficial edema. Bioelectrical impedance is also a water-specific technique, but it is mainly applicable for peripheral edema and has limitations to quantitate tissue total water content.

A new water-specific technique (MoistureMeter-D)

A primary requirement for the edema measurement is that the technique must be water-specific for whole tissue water. This is not an easy requirement since extracellular space contains free water and bound (or motionally restricted) water on the surface of macromolecules. Since electrical properties of free and bound water are different, the system should operate at frequencies where electrical properties of free and bound water are similar (i.e. whole water compartment is measured). This occurs at around 300 MHz. Measurement of the so-called dielectric properties at 300 MHz is highly dependent on changes in total water content and thus on edema.

Additional requirements include the possibility for local and generalized measurements practically at any anatomical site and user-selectable depth easily and quickly. Fig. 1 summarizes the measurement principle and illustrates the instrument with probes of different sizes.
MoistureMeter D - Background

Principle
The tissue is exposed to a 300 MHz low power electromagnetic (EM) wave.
A portion of the energy of EM wave is absorbed by tissue water.
The reflected wave contains information on tissue water content.

On measured dielectric properties, 
dielectric constant is directly proportional to tissue water content.

The system has been validated in patients with hemodialysis treatment (Nuutinen et al. Physiol Meas 25:447-454,2004). During fluid removal (1800-5000 ml, average 3100 ml) the tissue dielectric constant being directly proportional to tissue water content was measured together with circumference of the upper forearm. Sensitivity of a new dielectric device was 4-fold compared with traditional technique. Since the coefficient of variation for a single measurement was 2.0 % and for long-term measurements 5.0 %, small changes in tissue water content were detectable.

Early results and discussion

Fig. 2 illustrates breast tissue water content after breast-saving surgery and conventionally fractionated RT up to 50 Gy. An initial increase in water content is seen at 4-7 months after RT (Lahtinen et al, unpublished). Subcutaneous induration accounts for the elevation demonstrated at two years (Nuutinen et al, Radiother Oncol 47;249-254,1998) (Fig. 3).
**Fig. 2.** Breast tissue edema compared to the contralateral side after breast-saving surgery and conventionally fractionated RT up to 50 Gy.

**Fig. 3.** Subcutaneous fibrosis (0 = no, 1 = slight, 2 = moderate, 3 = severe) is related to increased tissue water content at 2 years. Increase of tissue water content is illustrated using a pre-RT measurement as a reference (BL).
Fig. 4. Lymphedema secondary to breast cancer treatment assessed by MoistureMeter-D at various depths (0.5, 1.5, 2.5 and 5 mm) can easily be detected as an increase of dielectric constant. Reference method was a segment volume technique.

Based on the assessment of lymphedema secondary to breast cancer treatment by MoistureMeter-D, Mayrovitz et al, (ISBS 2005) concluded that the dielectric method may serve as a rapid quantitative assessment procedure for documenting lymphedema (Fig. 4) and early detection of incipient lymphedema that is not yet clinically observable.

As a conclusion, edema is a common side effect in cancer therapy. Objective quantitation of edema has been extremely difficult due to the lack of suitable water-specific techniques. A sensitive water-specific device MoistureMeter-D (Delfin Technologies Ltd, Kuopio, Finland) is now available for the assessment of cancer treatment-related local and generalized edema, lymphedema and edema that is not yet clinically detectable.

*Modified from lecture presented in: 8th Biennial ESTRO Meeting on Physics and Radiation Technology for Clinical Radiotherapy, 24-29 September 2005, Lisboa, Portugal*