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Suction Blisters for the Investigation of Radiation Reactions in Human Skin

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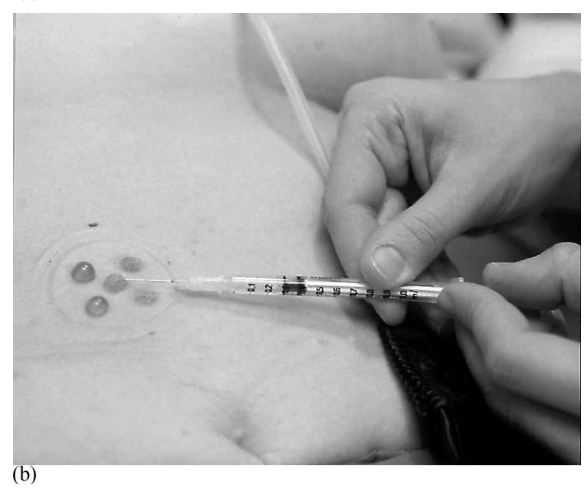
To the Editor

Subcutaneous fibrosis is a common, late complication of radiation therapy. The factors responsible for the development of the fibrotic reaction have not yet been well established, nor has the postirradiation ratio of skin collagen synthesis and degradation been adequately described. Although short-term and long-term changes in type I and III collagen synthesis of the human skin have been described (1, 2), their role in the development of palpable induration is not totally understood. Recently, an increase in the turnover of type I collagen and resulting accumulation of cross-linked type I collagen has been found (3) but the applied biopsies from irradiated skin are often considered invasive to the patient. Therefore, non-invasive tools to investigate the basic mechanisms of radiation action are required.

Although subcutaneous fibrosis is rarely a major clinical problem with the present techniques and treatment units, skin fibrosis is a useful tool in the study of the fibrotic reaction in general and the relationship between acute and late radiation reactions (4). Intense acute and late skin reactions can be found in patients receiving high radiation doses to the skin, such as high-energy electron beams, photon or electron beams with bolus and tangential beams in the head and neck region and in the axillar region related to breast cancer radiotherapy.

Induction of suction blisters of the skin and the subsequent measurement of collagen metabolism markers from suction blister fluid (SBF), i.e. skin interstitial fluid, have mainly been applied in dermatological investigations (5, 6). Recently, Autio et al. (1) demonstrated for the first time in vivo the increased collagen synthesis by analyzing type I and III procollagen propeptide concentrations in SBF of the skin, 1–5 years after postmastectomy radiotherapy. Accordingly, the levels of type I and III aminoterminal (PINP and PIIINP, respectively) and type I carboxyterminal (PICP) procollagen propeptides were considerably increased in comparison with the non-irradiated control breast skin. Autio et al. (1) used a hospital air pressure system to maintain an underpressure of about 350 mbar in the purpose-built suction cups. Typically, a suction time of 60–90 min was enough to induce suction blisters. Epidermis will separate from the basement membrane and the resulting space (blister) is filled with interstitial fluid. Underpressures higher than 350 mbar as well as elevation of the temperature may induce the blisters more quickly (7). However, elevated underpressure

(a)



(b)

Fig. 1. a) The portable suction blister device used for inducing suction blisters in three body sites. b) Five simultaneous suction blisters in abdominal skin. The suction blister fluid (SBF) is collected using a fine needle.

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may result in rupture of the blister and small vessels of the upper dermis.

Although the suction blisters can be induced by the air pressure systems typically available in hospitals, a portable bedside system allows one to induce blisters without restrictions on the site of the hospital air pressure outlets. Therefore, a light-weight instrument dedicated for producing radiation-induced suction blisters in the skin (Fig. 1a) is now available (Ventipress Ltd., Lappeenranta, Finland). The system can accurately maintain an underpressure of 200–400 mbar. Four specially designed suction blister cups (Ventipress Ltd., Lappeenranta, Finland) can simultaneously be connected to the pressure unit. One suction cup enables five simultaneous blisters (Fig. 1b) producing a total volume of up to 0.8–1.0 ml SBF.

Autio et al. (1) demonstrated that the method causes no permanent skin damage in patients 1–5 years after radiotherapy. After fluid collection, the stretched epidermis (i.e. the roof of the blister) covers the subepidermal tissues while new epidermis grows underneath and the old one is removed by desquamation. The skin site heals in a few days and a slight pigmentation can be seen until 2–4 weeks after blister induction but without permanent scarring. Recently, Keskikuru et al. (2) induced suction blisters with irradiated and non-irradiated skin during radiotherapy using this new device, without any adverse effects or pain to the patients. Quite the contrary in fact, since the suction blister sites in irradiated skin were found to heal faster than the blister sites in the contralateral non-irradiated side, which is most likely related to radiation-induced accelerated repopulation of epidermal basal cells.

Although we have used the suction blister device mainly for the investigation of late effects of radiotherapy in the skin and subcutaneous tissues, the device and the collected SBF enable the investigation of the role of several radiation-induced mediators such as growth factors and cytokines in the development of acute and late radiation reactions.

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