Field cancerization is characterized by the macroscopic occurrence of multiple precancerous and/or cancerous lesions in a field exposed to high doses of an environmental toxin such as ultraviolet (UV) radiation. At the invisible level, macroscopic field cancerization is preceded and accompanied by the development of large numbers of mutations. In the case of UV-induced field cancerization, typical C-to-T or CC-to-TT tandem transitions at dipyrimidine sites (i.e. UV fingerprint mutations) in the tumour suppressor gene TP53 (also known as p53) being the primary cause of nonmelanoma skin carcinogenesis. Indeed, in sun-exposed skin, mutations at particular codons of TP53 are present at frequencies of $10^{-6}$ to $10^{-2}$ and the number of TP53 clonal patches that are 60–3000 cells in size exceeds more than 30 patches per cm$^2$. A perfect treatment of field cancerization should not only destroy the visible cancerous or precancerous lesions but also eliminate the abnormal, invisible preclinical alterations being linked to mutations in genes such as TP53, thereby reducing the de novo occurrence of cancer in the field.

The modern era of noninvasive treatment for field cancerization in dermatology began with the introduction of the smart concept of photodynamic therapy (PDT) employing photosensitization with endogenous porphyrins induced by exogenous administration of ample amounts of aminolaevulinic acid (ALA). The concept was pioneered by the work of Kennedy et al., followed quickly by us and others. When we introduced ALA-PDT nearly three decades ago on a case-to-case base into the clinic for the treatment of field cancerization and reported the first results, we set a question mark at the end of the title of the publication as we were uncertain whether the treatment would find its way into the therapeutic routine armamentarium for nonmelanoma skin cancers. In due course the question mark was erased and PDT became a standard in the treatment of field cancerization.

Over the years, other novel therapeutic agents including diclofenac sodium in hyaluronic acid, imiquimod and ingenol mebutate enriched the therapeutic armamentarium for the treatment of field cancerization of the skin. However, the recent introduction of the use of daylight in PDT advanced this treatment one step further, not only minimizing PDT pain (as one of the biggest disadvantages of conventional PDT) but also allowing exposure of very large, nearly unlimited fields, whereas fields are limited at least for some of the PDT drug competitors to 25 cm$^2$ according to medical license and prescription files. Direct comparisons of therapeutic agents for field cancerization are sparse but a meta-analysis revealed that conventional PDT is at least as effective as ingenol mebutate or imiquimod and more effective than diclofenac sodium in hyaluronic acid (but all of them are less effective than conventional topical 5-fluorouracil) in producing complete clearance of actinic keratoses (AK).

Beyond surgical curettage different physical pretreatments such as microneedling and (micro)dermabrasion have been used in order to potentiate the efficacy of PDT. Now Wenande et al., in this issue, report superior clearance (81% vs. 61%) of AKs of all grades in cancerized fields (>50 cm$^2$) and enhanced rejuvenating effects after methyl aminolaevulinate daylight PDT (dPDT) that was preceded by tailored skin pretreatment (according to the AK grade) using ablative fractional laser (AFL) [2940-nm erbium-doped yttrium aluminium garnet (Er: YAG)] compared with microdermabrasion using pads (with 58.5-μm diameter particles). Tailoring included removal of bulk portions of hyperkeratotic elements. For field-directed treatment, the immediate end points were erythema and pinpoint bleeding for both AFL and microdermabrasion. Notably, AFL treatment also led to fewer new AKs, suggesting that invisible clonal lesions containing TP53 mutations may have been eliminated by the approach, as implied for conventional PDT.

AFL-fortified dPDT may be a patient’s preferred choice for treatment of field cancerization because of its high efficacy and potential to treat large areas in one treatment session followed by a relatively short downtime (compared with smaller areas, i.e. $<25$ cm$^2$), and necessity of multiple therapeutic exposures, with longer downtimes in the case of treatment with topical agents such as ingenol mebutate or 5% imiquimod. However, several questions remain: do the long-term response rates of AFL-assisted dPDT hold up to the short-term results (at 3 months) of the present study? What is the exact efficacy of AFL-assisted dPDT in direct head-to-head comparison with ingenol mebutate or imiquimod treatment? And last but not least, can a nanoemulsion of ALA exceed the efficacy of methyl aminolaevulinate in AFL-assisted dPDT, as is the case in conventional PDT?
Conflicts of interest

P.W. has received speaker’s honoraria and/or travel grants/reimbursement in the past from Photocure ASA, Galderma and Biofrontera AG.

P. WOLF
Medical University of Graz, Auenbruggerplatz
8, A-8036 Graz, Austria
E-mail: peter.wolf@medunigraz.at

References