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Editorial Open Access

Multimodal Microscopy for Skin Cancer Diagnosis and Therapy Guidance

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Editorial

Skin cancer is an increasing burden on people of all ages. Among various types of skin cancers, basal cell carcinomas (BCCs) have the highest occurrence. About 2.5 million new cases of BCCs are diagnosed every year in the USA and another 500,000 in Europe and Australia [1,2]. BCCs occur most commonly in middle-aged and older people, but, lately, skin cancers are increasingly affecting younger people, too [3]. Approximately 80% to 90% of the cases occur on the head-and-neck, including 65% on the face, in high-risk anatomical areas such as on or near the nose, eyes, ears or mouth. Although not fatal, BCCs can cause large-scale anatomical destruction, resulting in morbidity, physical disfigurement, loss of function (breathing, hearing, swallowing and vision) and psychological trauma. Quality of life thus becomes a significant issue for these patients. Consequently, Mohs surgery guided by frozen pathology is performed to precisely remove the cancer with minimal damage to the surrounding normal skin [4]. Because Mohs surgery is guided by frozen pathology, the procedure is very effective at completely removing cancer, with five-year cure rates of 97% to 99%. However, the preparation of frozen pathology is labor-intensive and time-consuming, which results in the overall Mohs procedure being expensive. As incidence rates of skin cancer continue to increase, the number of physician visits and the number of Mohs surgeries in the USA nearly doubled during the last decade. Currently, an estimated 1.5 million surgeries are performed every year, with treatments costs exceeding $3 billion [5].

The increasing incidence and prevalence of BCCs, especially in an increasingly older population, combined with increasing costs has led to the search for and increasing adoption of newer alternative non-surgical treatments that can be less invasive and far less expensive. Such treatments include curettage-and-electrodessication, topical drug therapy, cryotherapy, photodynamic therapy, radio therapy, and laser ablation and/or coagulation [6,7]. The latest guidelines for the use of these alternative non-surgical treatments were issued by the National Comprehensive Cancer Network. Similar "appropriate use" guidelines were also issued by the American Academy of Dermatology, American Society for Dermatologic Surgery, American Society for Mohs Surgery and American College of Mohs Surgery. Non-surgical treatments are particularly well suited for superficial and nodular types of BCCs, which are shallow (depth ~ 200-500 μm) and less aggressive compared to the other deeper and more aggressive types (micronodular, infiltrative, sclerosing). The superficial and early nodular BCCs constitute about 40% of Mohs surgical cases (about 600,000 per year in the USA, another 200,000 in Europe and Australia) [8].

An important challenge for dermatologists is to accurately triage patients based on cancer type and stage (invasion depth), such that appropriate therapy can be applied. Superficial and early nodular BCCS are good candidates for non-surgical therapy [9-11]. However, non-surgical treatments do not produce tissue for pathological confirmation of clearance. Furthermore, due to the lack of traditional post-treatment pathology, the treatments are monitored with periodic clinical follow-up examination. This approach is reasonably taken because superficial and nodular BCCs are low-risk, slow growing, non-aggressive and non-metastatic cancers. However, the lack of pathological feedback results in variable long-term recurrence rates for non-surgical treatments (61% to 90%) [9-11]. Not surprisingly, the resulting variable efficacy and variable cure rates are major barriers against further advances toward routine and widespread use of these emerging alternative non-surgical treatments.

To address this challenge, non-invasive methods for real-time and reliable assessment of the lesion stage, and thus for triaging patients, guiding therapy and monitoring its effectiveness are needed.

Many studies have shown that optical imaging may help in improving the diagnosis of BCCs. Among various optical modalities, Optical Coherence Tomography (OCT) and Reflectance Confocal Microscopy (RCM) have shown the highest promise in BCC diagnosis. RCM provides cellular-level resolution images and therefore it can be used to accurately detect the morphological features of superficial and nodular BCCs and provide high diagnostic accuracy. RCM can also determine lateral margins.. On the other hand, OCT images deeper, to depth of ~1 mm into the reticular dermis, and can be used to detect deeper tumors that are beyond the reach of RCM, and delineate their deep margins. When used individually and independently, both OCT and RCM can noninvasively detect superficial and nodular BCCs with sensitivities and specificities in the range 80% to 95% and 70% to 90%, respectively [12-14]. Furthermore, other studies have reported the ability of OCT to reliably detect the depth of BCCs *in vivo* [15-20].

However, RCM images to a depth of ~200 μm, and determination of margins is possible only for tumors at the dermal-epidermal junction and within the papillary dermis in skin, while OCT sensitivity and specificity is yet to be validated in larger trials for accuracy and repeatability. Therefore, a new "game changing" approach is to combine these two modalities within the same instrument and benefit by the synergistic capabilities of both technologies. This approach has been recently demonstrated with high success by scientists and clinicians at Physical Sciences Inc. and Memorial Sloan Kettering Cancer Center (MSKCC) (see photograph of the instrument and RCM/OCT images in Figure 1) [21].

A study on over 100 cases has demonstrated the capability of this technology to provide 3-dimensional volumetric assessment of tumor morphology, at high resolution in real-time. The new multimodal imaging modality has demonstrated the possibility of RCM-OCT to guide triage of BCC types before treatment and confirmation of

clearance afterwards. These results clearly show a path forward towards clinical adoption of the RCM/OCT technology. Furthermore, since both RCM and OCT imaging have been granted reimbursement codes, it is clear that that longer-term clinical acceptance and adoption of this proposed technology is very likely.

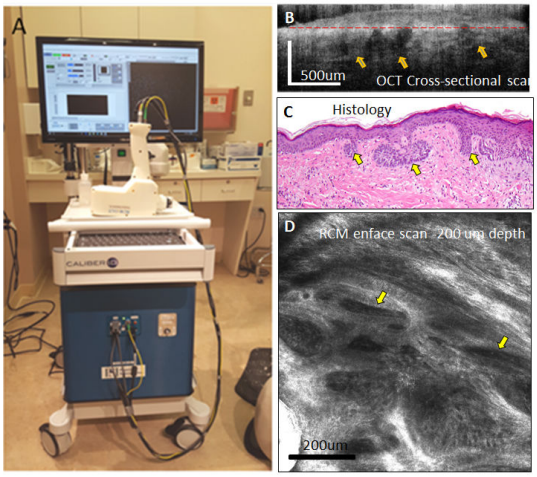

Figure 1 A Photograph of the RCM/OCT instrument; B- OCT image of a superficial nodular BCC; C- corresponding histology; D- RCM image taken at approximately 200 um from tissue surface. Arrows in the OCT and histology indicate tumor location, while in the RCM the arrows indicate cell palisading, as indicative of BCC presence.

In conclusion, multimodal microscopy seems to be a new standard in cancer diagnosis and therapy guidance. Besides skin cancer, it can be applied to other cancers such as oral, cervical, and potentially to gastro-intestinal cancers.

References

1. Lomas A, Leonardi-Bee J, Bath-Hextall F (2012) A systematic review of worldwide incidence of nonmelanoma skin cancer. Br J Dermatol. 166: 1069-1080.
2. Rogers HW, Weinstock MA, Harris AR, Hinckley MR, Feldman SR, et al. (2010) Incidence estimate of nonmelanoma skin cancer in the United States 2006, Arch. Dermatol. 146: 283-287.
3. Deady S, Sharp L, Comber H (2014) Increasing skin cancer incidence in young, affluent, urban populations: a challenge for prevention. Br J Dermatol 171: 324-331.
4. ViolaKV, Jhaveri MB, Soulos PR, Turner RB, Tolpinrud WL, et al. (2012) Mohs micrographic surgery and surgical excision for nonmelanoma skin cancer treatment in the Medicare population. Arch Dermatol. 148: 473-477.
5. Mudigonda T, Pearce DJ, Yentzer BA, Williford P, Feldman SR (2010) The economic impact of non-melanoma skin cancer: a review. J Natl Compr Canc Netw. 8: 888-896.
6. Choudhary S, Tang L, Elsaie ML, Nouri K (2011) Lasers in the treatment of nonmelanoma skin cancer. Dermatol. Surg 37: 409-425.
7. Amini S, Viera MH, Valins W, Berman B (2010) Nonsurgical Innovations in the Treatment of Nonmelanoma Skin Cancer. J Clin Aesthet Dermatol 3: 20-34.
8. Sierra AHC, Yelamos O, Chen CHJ, Rajadhyaksha M (2017) Reflectance confocal microscopy-guided laser ablation of basal cell carcinomas: initial in vivo results. Optical Biopsy XV: Toward Real-Time Spectroscopic Imaging and Diagnosis, Proceedings of SPIE 10060.
9. Iyer S, Friedli A, Bowes L, Kricorian G, Fitzpatrick RE (2004) Full face laser resurfacing: therapy and prophylaxis for actinic keratoses and non-melanoma skin cancer. Lasers Surg Med 34: 114-119.
10. Williams HC, Bath-Hextall F, Ozolins M, Armstrong SJ, Colver GB, et al. (2017) Surgery versus 5% imiquimod for nodular and superficial basal cell carcinoma: A 5-year results of the SINS randomized controlled trial. J Invest Dermatol, 137: 614-619.
11. Bahner JD, Bordeaux JS (2013) Non-melanoma skin cancers: Photodynamic therapy, cryotherapy, 5-fluorouracil, imiquimod, diclofenac, or what? Facts and controversies. Clin Dermatol, 31: 792-798.
12. Webber SA, Wurm EMT, Douglas NC, Lambie D, Longo C, et al. (2011) Effectiveness and limitations of reflectance confocal microscopy in detecting persistence of basal cell carcinomas: A preliminary study, Australas. J. Dermatol. 52: 179-185.
13. Rajadhyaksha M, Marghoob A, Rossi A, Halpern AC, Nehal KS (2016) Reflectance confocal microscopy of skin in vivo: From bench to bedside. Lasers Surg Med. 49: 7-19.
14. Al-Arashi MY, Salomatina E, Yaroslavsky AN (2007) Multimodal confocal microscopy for diagnosing nonmelanoma skin cancers. Lasers Surg Med 39: 696-705.
15. Nori S, Rius-Díaz F, Cuevas J, Goldgeier M, Jaen P, et al. (2004) Sensitivity and specificity of reflectance mode confocal microscopy for in vivo diagnosis of basal cell carcinoma: A multicenter study. J. Am. Acad. Dermatol. 51:923-930.
16. Cheng HM, Guitera P (2010) Systematic review of optical coherence tomography usage in the diagnosis and management of basal cell carcinoma. Br J Dermatol 173: 1371-1380.
17. Olmedo JM, Warschaw KE, Schmitt JM, Swanson DL (2007) Correlation of thickness of basal cell carcinoma by optical coherence tomography in vivo and routine histologic findings: A pilot study. Dermatol Surg. 33: 421I-426.
18. Hinz T, Lin KE, Hornung T, Voth H, Fortmeier I, et al. (2012) Preoperative characterization of basal cell carcinoma comparing tumour thickness measurement by optical coherence tomography, 20-MHz ultrasound and histopathology. Acta Derm Venereol 92: 132-137.
19. Braunmühl TV, Hartmann D, Tietze JK, Cekovic D, Kunte C, et al. (2016) Morphologic features of basal cell carcinoma using the en-face mode in frequency domain optical coherence tomography. J Eur Acad Dermatol Venereol. 30: 1919-1925.
20. Boone M, Suppa M, Miyamoto M, Marneffe A, Jemec G, et al. (2016) In vivo assessment of optical properties of basal cell carcinoma and differentiation of BCC subtypes by high-definition optical coherence tomography. Biomed Opt Express 7: 2269-2284.
21. Iftimia N, Yélamos O, Chen CSJ, Maguluri G, Cordova M, et al. (2017) Handheld optical coherence tomography–reflectance confocal microscopy probe for detection of basal cell carcinoma and delineation of margins. Journal of Biomedical Optics 22: 076006.