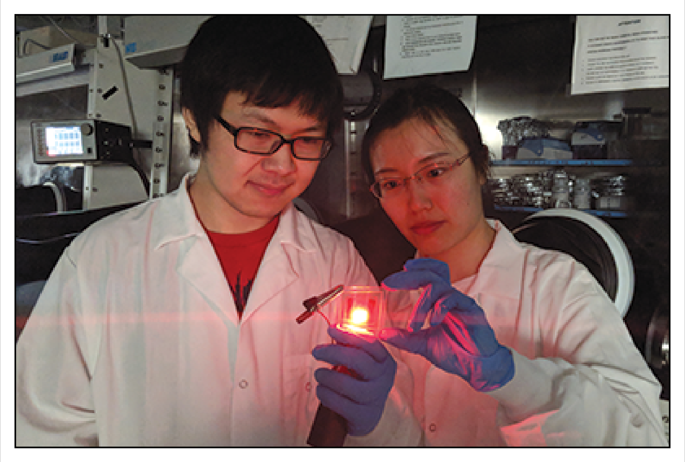
SOCIETY FOR INFORMATION DISPLAY NEWS

UCF Students Develop QLED Devices for Medical Applications

Photomedical researchers have been in search of low-cost, effective illumination devices with form factors that could facilitate widespread clinical applications of photodynamic therapy (PDT) or photobiomodulation (PBM). Student researchers from the University of Central Florida and other scientists recently discovered that ultrabright, efficient deep-red quantum-dot light-emitting devices (QLEDs) could fit nicely into this niche. Their recent paper in the Journal of the SID *(JSID) described how a photomedical approach based on these QLEDs could increase cell metabolism over control systems for PBM applications and kill cancerous cells efficiently for PDT applications.*

by Hao Chen and Juan He

At Display Week 2018, student authors Hao Chen, Juan He (both pictured below), their advisors Yajie Dong and Shin-Tson Wu, and collaborators Raymond Lanzafame, Istvan Stadler, Hamid El Hamidi, Hui Liu, Jonathan Celli, Michael R. Hamblin, Yingying Huang, Emily Oakley, Gal Shafirstein, and Ho-Kyoon Chung received the 2017 Outstanding Student Paper Award for "Quantum-Dot Light-Emitting Devices for Photomedical Applications." Chen, He, Wu, and Dong are with the College of Optics and Photonics (CREOL) and NanoScience Technology Center (NSTC) at the University of Central Florida. Lanzafame and Stadler are affiliated with the Laser Surgical Research Laboratory at Rochester General Hospital in Rochester, NY. El Hamidi, Liu, and Celli are with the Department of Physics at the University of Massachusetts Boston. Hamblin and Huang are with the Wellman Center for Photomedicine at Harvard Medical School in Boston, MA. Oakley and Shafirstein are with the Photodynamic Therapy Center at Roswell Park Cancer Institute in Buffalo, NY. And Chung is with the ITRC AMOLED Research Center at Sungkyunkwan University in Korea. Chen and He describe their research:



Student researchers Hao Chen (left) and Juan He (right) appear with the QLED device they developed for their award-winning project and paper.

Photomedicine is an emerging medical field in which light is used either to kill cancer cells with the assistance of photosensitizers and singlet oxygen or to stimulate cellular function leading to beneficial clinical effects. Both techniques, using laser or LED arrays, have been demonstrated as minimally invasive treatment strategies.[1]

Photomedicine has not, however, received widespread clinical acceptance mainly because of the lack of effective, low-cost illumination devices. Lasers and LED arrays are large and bulky. Organic light-emitting diodes (OLEDs), which offer a uniformly large-area light source and a thin, flexible, lightweight form, have been proposed for light-emitting bandage applications for PDT[2], but have been largely abandoned in favor of LEDs[3] because photomedical applications generally require light sources of relatively high luminance (>20,000 Cd/m^2 or ~10 mW/cm^2) at wavelengths in the deep-red region in order to have deep-tissue penetration while still maintaining sufficient energy for molecular excitation.[1] Existing OLEDs with either fluorescent or phosphorescent emitters cannot achieve such high luminance at the right wavelength windows because of significant efficiency roll-off problems at high current density4 and the lack of efficient deep-red emitters with narrow spectra.[5]

We began our research considering a promising alternative technology – electroluminescent quantum-dot light-emitting diodes (QLEDs), which have size-controlled tunable-emission wavelength and narrow emission spectra.[6] Among QLEDs of various colors, red are currently the most advanced and have demonstrated efficiency and luminance that rival or beat state-of-the-art thermal-evaporated red OLEDs, with narrow peak linewidths in the 20- to 30-nm range.

As shown in Fig. 1, the devices demonstrate a peak emission wavelength of 620 nanometers (nm), a narrow bandwidth of 22 nm, and can

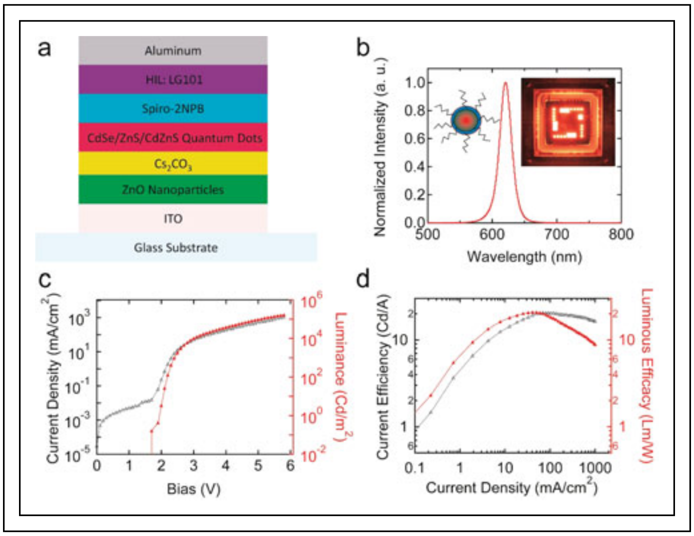


Fig. 1: *The above schematics and charts represent ultrabright, highly efficient, low roll-off inverted quantum-dot light emitting devices (QLEDs). (a) A schematic representation of the ultra-bright, high efficiency, inverted QLEDs. (b) Spectra of QLED electroluminescence. (c) Luminance and current density vs. driving voltage and (d) luminous efficacy and current efficiency vs. driving current density for typical devices. Adapted from data in reference.[7]*

achieve high current efficiency (20.5 Cd/A at ~20 000 Cd/m^2) and small-efficiency roll-off at high-driving current density.

Although the relatively short lifetime of these ultrabright deep-red QLED devices compared to state-of-the art OLEDs has limited their immediate applications in display or lighting markets, they are promising light sources for photomedicine, in which low-cost, wearable, disposable light-emitting bandage products are highly sought-after. And the narrow emission band and wavelength tunability of QLEDs enables them to more easily fit the emission spectrum into the absorption window of photosensitizers (for PDT) or cytochrome C (for PBM). Note: For our QLEDs, the LT50 at 2,000 nits or 100 nits initial luminance is estimated to be 350 hours or 7,000 hours respectively. The failure mode of QLED is not yet fully understood.

Our paper presented preliminary PBM and PDT results using these ultrabright red QLEDs as excitation light sources, with parallel studies using inorganic LEDs as comparisons. We also discussed the possibility of tuning QLED wavelength for targeted photomedicine, the development of flexible QLEDs, and their potential impact to wound repair or cancer treatment.

Finding a Suitable Problem

For our research team at the University of Central Florida, this was a typical "solution looking for a problem" process. Our group had developed high-performance red QLEDs with ultra-high luminance, narrow emission spectra, and a tunable wavelength range, but the device lifetime was limited. These QLEDs were not yet ready for display applications.

We were looking instead for applications that could make full use of the merits of our devices without our having to solve the lifetime issue yet. The early work of Lumicure (a UK company now called Ambicare Health) caught our attention. Their researchers tried to use OLEDs as flexible-light emitting bandages for the phototherapy of skin cancers. The idea was cool, but the results were not that satisfactory, because the relatively low power density and broad spectra of OLEDs can't meet phototherapy's stringent requirements. We thought, aha, that is where we can do better and the doctors don't need a bandage that lasts forever, so our lifetime issue won't be a problem. That is how we got started.

Because of the truly interdisciplinary nature of this project, we needed many partners from both the OLED and photomedicine communities. To connect with the photomedicine doctors, we went to the annual conference of American Society for Laser Medicine and Surgery (ASLMS) and showed our prototype QLEDs to physicians who were using red light in their practice. They were excited to see the color and brightness of our QLEDs and were happy to start some preliminary cell studies with us even if we only had small rigid QLEDs on glass at the time. The preliminary results were very promising. With these results, we then introduced the concept to the OLED community at Display Week and the OLED Summit to seek support for making flexible devices.

Preliminary PBM Results

We initially developed a 4-pixel (4 × 4-mm each.) QLED array as a photomedical light source. As shown in Fig. 2, a specialized platform/cradle was built to stabilize the QLED array, allowing proper tray positioning underneath cell cultures for in-vitro PBM and PDT experiments. The results were compared with control cell cultures that received no light treatment or parallel studies with inorganic LED treatment.

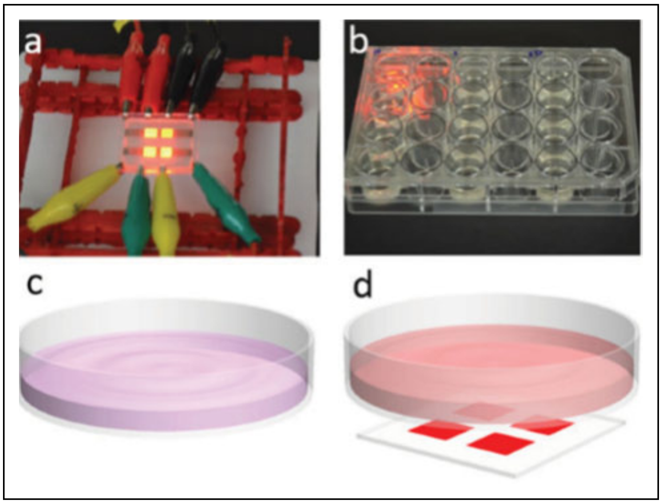


Fig. 2: *The experimental setup for photomedical testing included (a) a 2 × 2 red QLED array; (b) an experimental setup; (c) control cell cultures without light treatment; (d) cell cultures using QLED as a light source.*

For PBM testing, we used three cell lines cultured in 24-well trays. Photoradiation was performed using the ultrabright QLED to deliver 4.0 J/cm^2 to the culture wells during a 10-minute "treatment" at a power density of ~8 mW/cm^2. Control cell cultures received no light treatment. Cell metabolism was assessed using a 3-(4,5-dimethylthiazol-2yl)-2,5-diphenyltetrazolium bromide assay (Chemicon International Inc., Temecula, CA) 24 hours after treatment. (The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay is a colorimetric assay and is a popular method for evaluating cell metabolic activity.)

Parallel studies were performed at 670 nm ± 20 nm using an LED device (Quantum Devices, Barneveld, WI) delivering 4.0 J/cm^2 for 10 minutes' duration for comparison with the QLED PBM. Assay results at 24 hours showed that QLED PBM increased cell metabolism in one cell line and in a similar fashion to a NASA LED source.[8] Although the peak wavelength of QLED (~620 nm) is still not up to the ideal 660 nm for PBM, the results of QLED BPM are comparable with the LED PBM. Further tuning of the emission wavelength of QLED is expected to lead to improved PBM results.

Preliminary PDT Results

To evaluate the potential of red QLEDs as a light source for PDT, we used 3D cultures of A431 cells (a human cell line frequently used in cancer-associated biomedical studies.) Cultures were treated using either the QLED sources with low average irradiance (approx 1.8 mW/cm^2) or a solid-state LED with similar spectral emission but higher irradiance (approximately 130 mW/cm^2). Dosimetry was controlled so that cultures received the same total light dose of 30 J/cm^2 over the course of either 4.75 hours (QLED) or 4 minutes (solid state LED). Treatment response was evaluated 24 hours after PDT using an imaging-based approach.[9] Both QLED and LED sources achieved photodestruction of 3D tumor nodules, while quantitative image processing of multiple replicates revealed that PDT efficacy was slightly enhanced using the QLED source, with residual tumor viabilities of 0.61 +/ 0.04 versus 0.53 +/ 0.08 for the solid state and QLED sources respectively. This result is consistent with previous reports that PDT at low dose rates may be more effective and is significant here in view of the capability of the QLED to act as a low-cost, effective, and ergonomic source for PDT light activation over extended periods. These in-vitro studies are the first to demonstrate PBM and PDT using a QLED device and should pave the way for further developments in QLED-based photomedicine.

Wavelength Tunable Red QLED for Targeted Photomedicine

It should be noted that these promising preliminary results were obtained with ultrabright red QLED with a peak wavelength of ~620 nm. While this wavelength falls into the favorite range for most photomedical applications (620 to 670 nm), highly effective phototherapy calls for better wavelength-specific spectral control to maximize the absorption for photosensitizers (for PDT) or cytochrome C (for PBM) from QLED. By tuning the synthesis conditions (QD size and composition), we can achieve ultrabright QLEDs with precisely controlled emission peaks at specific wavelengths for wound repair and cancer treatment applications. Currently, such precise wavelength control can only be realized by expensive, bulky lasers, although the laser light needs to be waveguided with optical fibers and spread out with diffusers for large-area applications. Compared to lasers, QLEDs have clear advantages as low-cost, large-area, and wearable light sources, such as shown in a rendering in Fig. 3.

Facing Challenges, Lessons Learned

The key technical challenges of this project resided in its inherently multidisciplinary nature. The work required deep understanding and close collaborative progress with regard to QLED device performance, medical treatments, and regulatory approval processes. Another challenge, political in nature, lies in the public concerns about the cadmium contained in QD materials. Such concerns may be eased by serious medical evaluation of the QLED's beneficial treatment effect and the monitoring of any possible side effects.

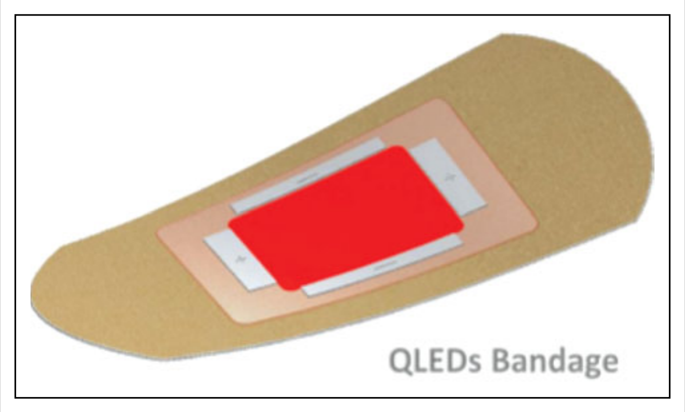


Fig. 3. *A QLED-based bandage for photomedicine applications might look like the rendering above.*

The biggest lesson we learned from this work was how to effectively conduct teamwork among many parties; that is, utilizing the specialty of each party and coordinating the whole team to move forward together. It was a vast communication project. Strong interest from both photomedicine and OLED communities were the key to help us maintain great working relations with both parties.

Working Toward a Flexible Implementation

Now we are looking forward to moving this project further ahead with real flexible QLEDs. Rigid QLEDs on glass substrates have been demonstrated to be effective in wound repair and cancer treatment in in-vitro tests. We now need to fabricate flexible QLED products on plastic substrates, with technical assistance from those in the flexible OLED field, and then demonstrate the therapeutic effects of the flexible QLEDs in-vivo.

We are now working on fabrication of flexible QLED prototypes with large active area and improved stability. Using the newly developed QLED prototypes, we are also collaborating with our photomedical partners to carry out preclinical in-vitro studies for treatments of several specific medical conditions, including oral cancers and diabetic wounds.

Our preliminary PBM and PDT results should pave the way for using the bright, pure-color red QLEDs in rigid or flexible form factors to positively affect phototherapy applications in dermatology, oncology, minimally invasive surgery, stroke, and brain disease, among other fields. We believe that this QLED-based technology, initially developed out of strong interest from the information display industry, can make inroads into new medical areas and have a direct, beneficial impact to mankind by radically changing the ways we manage cancer, acute and chronic wounds, inflammation, and antimicrobial resistance, to mention only several potential uses for photomedicine. The experience and knowledge gained in this project and the successful commercialization of QLEDs in the niche photomedical lighting market could help enhance QLEDs' stability and eventually enable their applications in display and/or general lighting.

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