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					19b. TELEPHONE NUMBER
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RPPR Final Report
as of 21-Jul-2023

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Title: Portable quantum dot electroluminescent (QDEL) light sources for point of care photodynamic treatment of deep wound MDR infections
Begin Performance Period: 10-May-2022 **End Performance Period:** 09-May-2023
Report Term: 0-Other

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STEM Degrees: 0 **STEM Participants:** 3

Major Goals: The primary objectives of our STTR Phase I project were to develop reliable, flexible, and lightweight quantum dot electroluminescent (QDEL) light sources, and to demonstrate the effectiveness of these portable QDEL devices in treating multidrug-resistant (MDR) bacteria through in-vitro antimicrobial photodynamic therapy (aPDT) studies. Our previous work with rigid on-glass QDEL devices has shown their efficacy in destroying MDR pathogens, outperforming antibiotics. However, while flexible QDEL (fQDEL) devices have been fabricated, their reliability and performance were not yet on par with rigid devices, limiting their application as an aPDT light source.
To determine the feasibility of using portable QDEL light sources for point-of-care aPDT applications, our Phase 1 project aimed to answer two technical questions: 1) Can lightweight fQDEL devices achieve similar reliability, efficiency, and optical power density (OPD) performance as their rigid counterparts through the engineering of polymer substrate and barriers? 2) Can fQDEL device-based aPDT demonstrate bactericidal effects in-vitro, and achieve high efficacy against both gram-positive (G+) and gram-negative (G-) MDR pathogens without inducing drug resistance?

Accomplishments: Accomplishment under Goals
Three main milestones were achieved with the joint efforts of QLEDCures, Hasan Lab at the Massachusetts General Hospital, Wellman Center for Photomedicine and Harvard Medical School (MGH/WCP/HMS) and Dong Lab at the University of Central Florida (UCF). First, we demonstrated that our QDEL devices are 10-1000 times more potent than state-of-the-art flexible organic light-emitting diode (OLED) devices in killing wound pathogens. Second, we significantly improved the reliability and performances of fQDEL devices using advanced barrier technologies. Lastly, we convincingly demonstrated the feasibility of QDEL-based aPDT for treating MDR wound infections by achieving potent aPDT eradication of both G+ and G- MDR bacteria using these reliable QDEL devices. Here we summarize the most relevant outcomes achieved during Phase I of the project and put these into perspective for Phase II.
1. Demonstration of superior QDEL aPDT compared to state-of-the-art OLEDs (QLEDCures/MGH)
Figure 1 shows the aPDT performance comparison of current commercial OLEDs with our rigid glass QDEL devices, when tested under the same treatment parameters. The OLEDs were commercial flexible devices obtained from Konica Minolta (KM), and the rigid QDEL devices were fabricated by QLEDCures/UCF. These rigid QDEL devices were developed and patented by QLEDCures/UCF before the project began 1.
As demonstrated in Figure 1, our QDEL devices are 10 - 1000 times more potent than commercial OLEDs for killing E. Coli (G-) and S. aureus (G+), respectively. The successful demonstration of the effectiveness and superiority of QDEL aPDT testing by MGH/WCP/HMS marked achievement of milestone 1 and provided

justification to execute milestone 2. This was crucial to validate the transfer of the functional structure of rigid QDEL to flexible devices, simplifying subsequent development focused solely on optimizing the flexible substrate and barrier encapsulation of fQDEL devices.

2. Significant improvements of fQDEL device performance and reliability (QLEDCures/UCF)

The second milestone of our project involved addressing the challenges encountered during the fabrication of preliminary fQDEL devices, mainly related to the barrier and thermal properties of the substrates and encapsulation materials used.

Figure 2 summarizes the optimization of the plastic substrate and flexible barrier layers to simultaneously improve the barrier property, performance, and thermal management of fQDEL devices. Both the material composition and the thickness of the substrate and barrier layers were evaluated experimentally and optimized. Substrate optimization included testing of transparent polymer- and thin glass-based substrates, and the pretreatment conditions of the substrates. Encapsulation optimization included the testing of polymer- and metal-based barriers, and the evaluation of different encapsulation methods, mainly barrier lamination and in-situ barriers fabricated by atomic layer deposition. Finally, these optimizations led to the best performance fQDEL devices shown in Figure 2, achieved by using a transparent indium tin oxide on polyethylene naphthalate (ITO/PEN) substrate, lamination of a 3M plastic-based barrier on the bottom, and a 3M metal foil on the top of the devices. The pretreatment conditions of the plastic-based 3M barrier and the 3M metal foil were also optimized.

Importantly, this second stage enabled fQDEL devices with 1) > 1-month shelf-life in ambient air, i.e., with no dark spots or optical power density (OPD) decay; 2) high current density and OPD at a low driving voltage and longer operating lifetime; and 3) low operating temperature which simultaneously enables the result mentioned in (2) and facilitates the safe use of the fQDEL devices on human skin. A reliable, low-cost, thin, and lightweight wearable bandage system could be developed using these fQDEL devices, as they are extremely thin, measuring only 0.2 to 0.3 mm in thickness and weighing approximately 1-2 grams. Moreover, these devices can be manufactured at a cost of less than 10 dollars, further highlighting their affordability and potential for integration into a bandage system. These results marked achievement of milestone 2 and paved the way towards aPDT testing of these fQDEL devices in-vitro.

3. Demonstrations of potent aPDT treatment of MDR bacteria using fQDEL device (MGH)

Successful aPDT treatment of MDR bacteria was demonstrated using the reliable fQDEL devices developed in the previous stage. Gram-positive MDR bacteria Staphylococcus aureus and gram-negative MDR bacterial species (Pseudomonas aeruginosa) were used, with methylene blue (MB) as the photosensitizer (PS). As shown in Figure 3, the survival of bacteria was significantly reduced after the aPDT treatment. Specifically, there was an ~ 6 logs decrease compared to the control group for G+ bacteria, and ~2-3 log reduction for G- bacteria at the tested parameters. These in-vitro results demonstrated the potent antimicrobial efficacy of our fQDEL devices against bacterial pathogens.

Conclusion

In summary, our study has successfully demonstrated the feasibility of creating low cost, light weight fQDEL devices that are reliable and exhibit potent aPDT efficacy against various MDR bacteria, surpassing the current standard of care. This achievement represents a significant step towards the development of wearable QDEL-based aPDT bandage systems, which can be further evaluated in aPDT studies in-vivo. Importantly, our results provide a strong foundation for Phase II wearable system development and future clinical studies, highlighting the potential commercial applications of this technology.

Please refer to the Uploaded files for the figures.

Training Opportunities: Nothing to Report

Results Dissemination: To keep the technology commercially competitive. We have not openly presented the technical details in conferences.

Honors and Awards: Nothing to Report

Protocol Activity Status:

Technology Transfer: QLEDCures has signed option agreement with UCF for exclusively licensing the patent "91.Y. J. Dong*, H. Chen+, S. T. Wu, J. He+, Quantum Dot Light Emitting Devices (QLEDs) and Method of Manufacture, Provisional Patent filed on September 29, 2017 as Serial No. 62/565,253. Nonprovisional Patent filed on September 26, 2018 as Serial No. 16/143,068; Patent (10593902) granted on March 17, 2020".
One more patent application on QDEL based aPDT bandage is in preparation.

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Person Months Worked: 3.00 **Funding Support:**
Project Contribution:
National Academy Member: N

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Project Contribution:
National Academy Member: N

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Project Contribution:
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National Academy Member: N

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National Academy Member: N

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Participant: Shruti Jayaprakash Saiji

Person Months Worked: 6.00 **Funding Support:**
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National Academy Member: N

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Project Contribution:
National Academy Member: N

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Partners

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RPPR Final Report
as of 21-Jul-2023

I certify that the information in the report is complete and accurate:
Signature: Joshua Wang
Signature Date: 5/16/23 10:55AM

Accomplishment under Goals

Three main milestones were achieved with the joint efforts of QLEDCures, Hasan Lab at the Massachusetts General Hospital, Wellman Center for Photomedicine and Harvard Medical School (MGH/WCP/HMS) and Dong Lab at the University of Central Florida (UCF). First, we demonstrated that our QDEL devices are 10-1000 times more potent than state-of-the-art flexible organic light-emitting diode (OLED) devices in killing wound pathogens. Second, we significantly improved the reliability and performances of fQDEL devices using advanced barrier technologies. Lastly, we convincingly demonstrated the feasibility of QDEL-based aPDT for treating MDR wound infections by achieving potent aPDT eradication of both G^+ and G^- MDR bacteria using these reliable QDEL devices. Here we summarize the most relevant outcomes achieved during Phase I of the project and put these into perspective for Phase II.

1. Demonstration of superior QDEL aPDT compared to state-of-the-art OLEDs (QLEDCures/MGH)

Figure 1 shows the aPDT performance comparison of current commercial OLEDs with our rigid glass QDEL devices, when tested under the same treatment parameters. The OLEDs were commercial flexible devices obtained from Konica Minolta (KM), and the rigid QDEL devices were fabricated by QLEDCures/UCF. These rigid QDEL devices were developed and patented by QLEDCures/UCF before the project began [1].

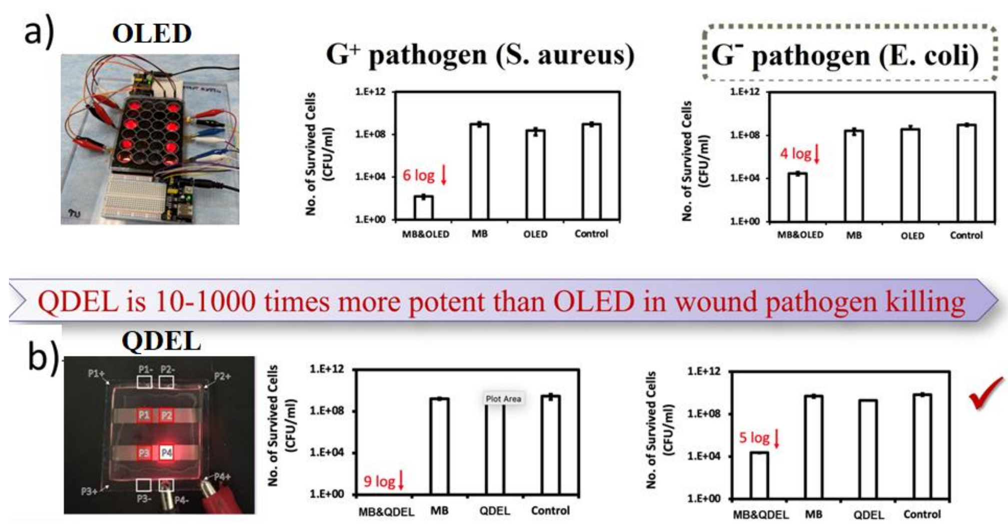

Figure 1. In-vitro antimicrobial efficacy test platform (left) and aPDT performance (right) for a) current commercial flexible OLEDs and b) our rigid glass QDEL devices. MB (methylene blue) is the photosensitizer.

As demonstrated in **Figure 1**, our QDEL devices are 10 - 1000 times more potent than commercial OLEDs for killing E. Coli (G^-) and S. aureus (G^+), respectively. The successful demonstration of the effectiveness and superiority of QDEL aPDT testing by MGH/WCP/HMS marked achievement of milestone 1 and provided justification to execute milestone 2. This was crucial to validate the transfer of the functional structure of rigid QDEL to flexible devices, simplifying subsequent development focused solely on optimizing the flexible substrate and barrier encapsulation of fQDEL devices.

2. Significant improvements of fQDEL device performance and reliability (QLEDCures/UCF)

The second milestone of our project involved addressing the challenges encountered during the fabrication of preliminary fQDEL devices, mainly related to the barrier and thermal properties of the substrates and encapsulation materials used.

Figure 2 summarizes the optimization of the plastic substrate and flexible barrier layers to simultaneously improve the barrier property, performance, and thermal management of fQDEL devices. Both the material composition and the thickness of the substrate and barrier layers were evaluated experimentally and optimized. Substrate optimization included testing of transparent polymer- and thin glass-based substrates, and the pretreatment conditions of the substrates. Encapsulation optimization included the testing of polymer- and metal-based barriers, and the evaluation of different encapsulation methods, mainly barrier lamination and in-situ barriers fabricated by atomic layer deposition. Finally, these optimizations led to the best performance fQDEL devices shown in **Figure 2**, achieved by using a transparent indium tin oxide on polyethylene naphthalate (ITO/PEN) substrate, lamination of a 3M plastic-based

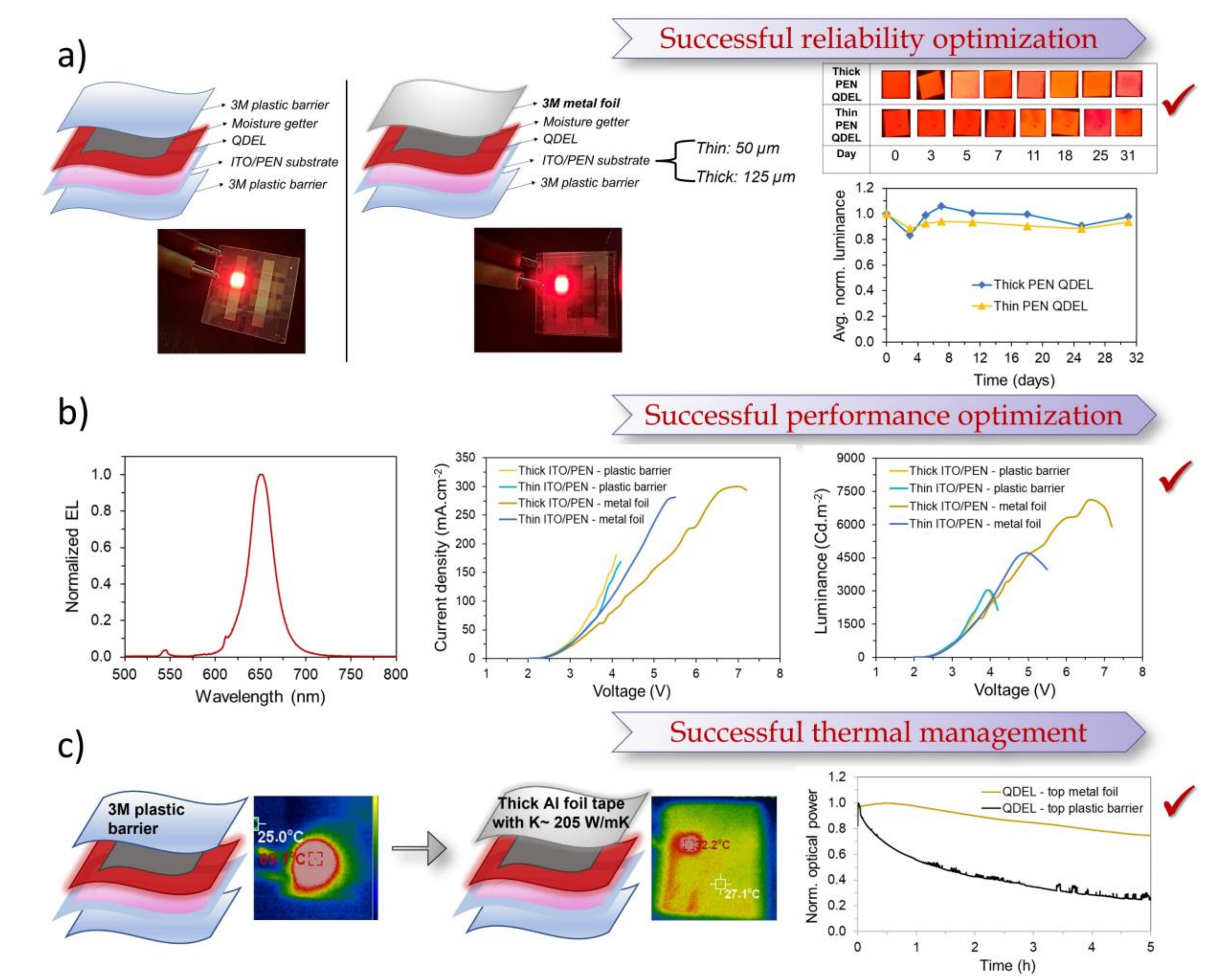

Figure 2. a) Structure of fQDEL devices encapsulated by bottom lamination of a 3M plastic film and top lamination of a 3M plastic film (left) or a 3M metal foil (middle). Evolution of the luminance and dark spots for pixels on fQDEL encapsulated with 3M plastic films and kept under ambient air. b) EL spectrum, J-V curves, and L-V curves of 651 nm fQDEL devices. c) Thermal photographs taken during operation of fQDEL devices encapsulated with a top plastic barrier (left) or a top metal foil (right). Lifetime test of fQDEL devices encapsulated with a top plastic barrier (black curve) or a top metal foil (golden curve) at 4 V.

barrier on the bottom, and a 3M metal foil on the top of the devices. The pretreatment conditions of the plastic-based 3M barrier and the 3M metal foil were also optimized.

Importantly, this second stage enabled fQDEL devices with 1) > 1-month shelf-life in ambient air, i.e., with no dark spots or optical power density (OPD) decay; 2) high current density and OPD at a low driving voltage and longer operating lifetime; and 3) low operating temperature which simultaneously enables the result mentioned in (2) and facilitates the safe use of the fQDEL devices on human skin. A reliable, low-cost, thin, and lightweight wearable bandage system could be developed using these fQDEL devices, as they are extremely thin, measuring only 0.2 to 0.3 mm in thickness and weighing approximately 1-2 grams. Moreover, these devices can be manufactured at a cost of less than 10 dollars, further highlighting their affordability and potential for integration into a bandage system. These results marked achievement of milestone 2 and paved the way towards aPDT testing of these fQDEL devices *in-vitro*.

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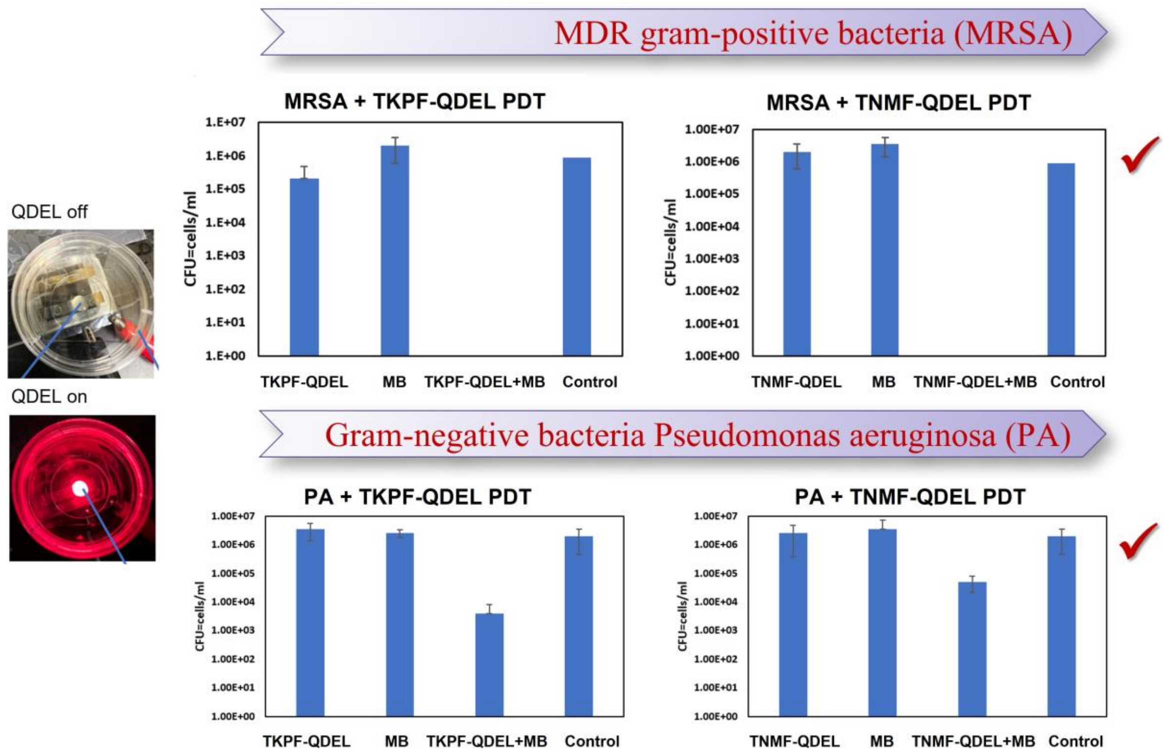

Figure 3. In-vitro aPDT treatment results for MDR gram-positive bacteria (MRSA) (up), and gram-negative bacteria (Pseudomonas aeruginosa, PA) (down). TKPF is a fQDEL device with thick ITO/PEN and top plastic film, while TNML is a device with thin ITO/PEN and top metal foil.

Conclusion

In summary, our study has successfully demonstrated the feasibility of creating low cost, light weight fQDEL devices that are reliable and exhibit potent aPDT efficacy against various MDR bacteria, surpassing the current standard of care. This achievement represents a significant step towards the development of wearable QDEL-based aPDT bandage systems, which can be further evaluated in aPDT studies *in-vivo*. Importantly, our results provide a strong foundation for Phase II wearable system development and future clinical studies, highlighting the potential commercial applications of this technology.