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● *Review Article*

TOTALLY IMPLANTABLE WIRELESS ULTRASONIC DOPPLER BLOOD FLOWMETERS: TOWARD ACCURATE MINIATURIZED CHRONIC MONITORS

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Abstract—Totally implantable wireless ultrasonic blood flowmeters provide direct-access chronic vessel monitoring in hard-to-reach places without using wired bedside monitors or imaging equipment. Although wireless implantable Doppler devices are accurate for most applications, device size and implant lifetime remain vastly underdeveloped. We review past and current approaches to miniaturization and implant lifetime extension for wireless implantable Doppler devices and propose approaches to reduce device size and maximize implant lifetime for the next generation of devices. Additionally, we review current and past approaches to accurate blood flow measurements. This review points toward relying on increased levels of monolithic customization and integration to reduce size. Meanwhile, recommendations to maximize implant lifetime should include alternative sources of power, such as transcutaneous wireless power, that stand to extend lifetime indefinitely. Coupling together the results will pave the way for ultra-miniaturized totally implantable wireless blood flow monitors for truly chronic implantation. (E-mail: Esejdic@pitt.edu) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Battery-less, Blood flow monitor, Flowmeter, Free flap, Wireless power, Transcutaneous wireless power.**

INTRODUCTION

Microvascular free flap (MFF) surgeries are a class of procedures used in reconstructive surgeries to correct anatomic defects requiring persistent monitoring to ensure surgical success (Hong et al. 2014; Kang et al. 2013; Zhou et al. 2014). MFF surgeries involve the transfer of a tissue block (*i.e.,* flap) from one part of the body (*e.g.,* thigh, buttocks) to another (*e.g.,* breast, mandible). The arteries, veins, and other connective tissues of the donor tissue are connected to those at the transfer site. The microvascular connections, called anastomoses, establish blood flow to the transferred tissue block (Goodstein and Buncke 1979; O'Brien et al. 1974). Anastomotic failures (caused by clotting, leaks, *etc.*) hinder blood flow to the transferred tissue. Unless these failures are caught, the tissue will certainly die (Chen et al. 2007; Wu et al. 2013). MFF monitoring by trained technicians is a necessity to reduce the death of tissue and subsequent risky surgical re-exploration. Of the many MFF monitoring technologies available, few can provide an accurate, easy-to-use and cost effective combination.

All MFF monitoring techniques need to be accurate; false positives and false negatives lead to costly and risky surgical re-exploration. Ease of use can be a limiting factor in a monitoring technology's adoption, particularly when the technology requires skilled technicians and prevents patient mobility. Early and quick detection (*i.e.,* through monitoring) of the nearly 10% to 20% of compromised vessels in free flaps has helped to increase flap salvage rates (Liu et al. 2012; Yu et al. 2009), which has led to the continued development and exploration of numerous monitoring technologies to minimize lost flaps.

Techniques to monitor MFFs are abundant, but many have fallen to disuse in favor of cheaper and more practical and easier-to-use alternatives that can service the gamut of applications. Buried flaps, vascularized bone grafts, pigmented skin flaps, skin grafted muscle flaps and flaps with small skin paddles are all challenges that a monitor must face with evaluation. Several monitors, such as the fluorescein monitor, thermocouple, photoplethysmography, the transcutaneous laser Doppler,

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and the transcutaneous PO_2 monitor have significant drawbacks that have led to their disuse (Swartz et al. 1988). Non-invasive near-infrared spectroscopy (NIRS) exhibited promise with its low false-positive and low false-negative rates. However, NIRS monitoring suffers from several drawbacks, including a slow response time, an inability to monitor buried flaps, a sensitivity to interfering light sources, and finally, its cumbersomeness (Lohman et al. 2013). Even newer monitoring methods such as positron emission tomography (Schrey et al. 2008) and micro-endoscopy (Upile et al. 2006) are considered cumbersome and impractical. The Cook–Swartz implantable Doppler device, however, offers significant advantages over its competitors. This device allows for direct-contact monitoring of a vessel, which increases the reliability of patency monitoring, particularly for buried free flaps (Disa et al. 1999).

Even though the wired implantable Doppler is considered the gold standard in MFF monitoring (Guillemaud et al. 2008; Oliver et al. 2005; Pryor et al. 2006; Rozen et al. 2011), it is not without its shortcomings (Cho et al. 2002; Paydar et al. 2010; Rosenberg et al. 2006), which can be mitigated through the employment of another Doppler technology, the wireless implantable Doppler (WID) (Gimbel et al. 2014; Rothfuss et al. 2016; Unadkat et al. 2014). This review focuses on *totally* implantable WID devices using piezo-electric transducers. The review excludes multichannel and multisensor devices (*e.g.,* Axelsson et al. 2007; Gräns et al. 2009; Kong et al. 2005), because of their additional size and power consumption, precluding comparisons with other WIDs. We review the major open problems toward developing WIDs for MFF and chronic implantation applications. Published solutions to these problems and the emerging and future directions to solve these problems follow.

CLINICAL BLOOD FLOW MONITORING: A BACKGROUND

Elements of an ideal monitor

The ideal microvascular blood flow monitor is easily deployable and easily interpretable by inexperienced operators, provides continuous and reliable monitoring, is tolerated by the patient and is applicable to any site (Smit et al. 2010). To date, according to Smit et al., the most promising monitors for free flap monitoring are the Cook–Swartz wired implantable Doppler, NIRS and laser Doppler flowmetry. Although NIRS and laser Doppler flowmetry are non-invasive and reliable, they are not applicable to all sites, nor easily interpretable like the wired implantable Doppler. However, the wired implantable Doppler suffers from reliability problems. No single technology has achieved these specifications fully, leaving the field open for solutions.

In cases of anastomoses, deployment simplicity and monitoring reliability have been addressed by using anastomotic flow couplers (Zhang et al. 2012). Major reliability problems with the wired Doppler probe stem from probe placement, as proper placement requires experience (Yu et al. 2009). The flow coupler conveniently incorporates the probe into the coupler's rigid ring wall to reduce the placement difficulties. The flow coupler can be rapidly deployed using a hand-held assembly. Recently, monitors have targeted the reliability problems and interpretation difficulties of the wired Doppler gold standard, which stem from its wire tether to a bedside monitor and lead to additional unnecessary surgery (Zhang et al. 2012), by eliminating the problematic wire tether and totally implanting the monitor (Rothfuss et al. 2016; Unadkat et al. 2015). True continuous monitoring requires an unlimited power source, which currently is found only in bedside monitoring (*i.e.,* those using wall outlets). In power constrained applications (*i.e.,* totally implanted wireless monitors), approximately continuous monitoring has been obtained by duty cycling the implant power-on/sensing time (Cannata et al. 2012; Rothfuss et al. 2016; Vilkomerson et al. 2008), often achieving years of approximately continuous measurement.

Invasive technologies, such as the implantable wired Doppler, are tolerable only in the short term, because of limiting patient mobility. To date, all totally implantable blood flow monitors remain overly large and intolerable to patients. The root of the non-ideal implant sizes is shared among: lack of advanced monolithic integration (*e.g.,* Di Pietro and Meindl 1978; Gill and Meindl 1975), power requirements (*e.g.,* battery size [Rothfuss et al. 2016; Vilkomerson et al. 2008; Yonezawa et al. 1992]), and implant antenna size (*e.g.,* telemetry [Vilkomerson et al. 2008] and/or wireless power transfer [Tang et al. 2014]).

Economics of monitoring and failures

The financial aspects of free flap monitoring and the cost associated with surgical re-exploration represent a barrier toward adoption of a monitoring technology. When free flap failure occurs, the financial costs are high. Fischer and colleagues' cost analysis for breast flaps, across 1303 flaps between 2005 and 2011, revealed that major surgical complications increased the length of stay to 6.14 d on average, with a total average cost of \$28,261, compared with no complications, which incurred 4.20 d on average and an average cost of \$19,106—a cost penalty of \$9155 and an increased stay of 1.94 d (Fischer et al., 2013). For head and neck flaps, Gupta's 2010 analysis (in Canadian dollars) revealed that failed flaps cost \$1413.73/d for an average stay of 34.5 d, compared with \$1327.71/d for an 18.8-d stay in successful free flap surgeries (Gupta, 2012), a difference of +\$23,812.74 for