

Optical assessment of genital changes associated with female sexual arousal: a mini-review

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Abstract

Background: Optical techniques, including laser Doppler flowmetry (LDF), photoplethysmography (PPG), and near-infrared spectroscopy (NIRS), are emerging as one of the most popular tools for female sexual arousal response (FSAR) assessment. However, to our knowledge, no narrative reviews have focused on the application of these optical techniques in FSAR assessment.

Aim: To fill out the existing gap, we review the literature regarding using optical techniques in FSAR assessment in preclinical and clinical studies.

Methods: A literature search was performed on the manuscript with terms including “female sexual dysfunction, FSAR, LDF, PPG, NIRS” between 1974 and 2024 using PubMed, Google Scholar, and MEDLINE. Among the articles identified, 18 articles were reviewed after excluding articles with non-relevant topics, duplicate articles, and articles not written in English.

Outcomes: This article reviews 11 studies that used LDF/imaging, four studies that used PPG, and three studies that used NIRS, including the employed experimental protocols in each study.

Results: Various optical techniques were used in FSAR assessment during electrical stimulation, visual and tactile stimulation, and drug administration. Additional studies, including using non-human primate models, testing the effects of different anesthetics on FSAR in preclinical studies, and performing more clinical studies to develop a standard for human FSAR monitoring using optical techniques that can lead to the use of optical techniques in clinical practices, could be considered. Meanwhile, non-contact systems and other optical techniques like optical coherence tomography, photoacoustic endoscopy, and Raman spectroscopy can be developed for future FSAR studies.

Clinical Translation: This article can provide a good overview of the preclinical and clinical investigations of FSAR using LDF, PPG, and NIRS. Understanding the differences between the techniques will allow clinicians to choose an appropriate technique for their FSAR studies.

Strengths and Limitations: This review is the first to overview various optical techniques used to evaluate FSAR. A limitation of the review is that there is no clinical study that uses NIRS for FSAR monitoring.

Conclusions: LDF/imaging, PPG, and NIRS have been used in various FSAR investigations. Such optical techniques have the potential to be used in future FSAR studies to quantitatively analyze the physiological changes during FSAR.

Keywords: female sexual dysfunction; female sexual arousal response; laser Doppler flowmetry; photoplethysmography; near-infrared spectroscopy.

Introduction

Female sexual arousal response (FSAR) is a multifaceted process influenced by physiological, psychological, and socio-cultural factors. Normally, FSAR induces physiological changes that include an expansion of the blood vessels, which allows more blood flow to the lower abdomen and genitals, resulting in vasocongestion. During FSAR, relaxation of smooth muscles in the vaginal wall and clitoral vasocongestion and engorgement also follow.¹ Vaginal lubrication, which is the results of the transudation of plasma in the vagina and secretions from uterus, Skene's and Bartholin's glands, can be evidence of FSAR.^{1,2}

To monitor physiological FSAR, non-optical and optical techniques are used.^{3–7} The non-optical techniques include assessing relevant hormones, ultrasonography, and magnetic resonance imaging. Meanwhile, the optical techniques include

laser Doppler flowmetry (LDF), laser oximetry or near-infrared spectroscopy (NIRS), and photoplethysmography (PPG). While the non-optical techniques are conventionally used to evaluate female sexual dysfunction, they have several disadvantages. Assessment of hormones associated with vaginal pH is performed by taking vaginal fluids from a tampon.^{8,9} Some studies reported vaginal fluid collection using a menstrual cup as well.^{10,11} While sample collection and analysis are straightforward, care must be taken since the sample is easily contaminated by urine, and the property of the sample changes as time passes.¹² Duplex Doppler ultrasonography has been able to record information during sexual stimulation.^{13,14} However, it is highly operator-dependent, and ultrasound images often have artifacts that can lead to misdiagnosis.¹⁵ Functional MRI (fMRI) enables clarification of the brain function that is correlated with

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sexual arousal and response.^{16,17} However, it is costly and cannot be used for subjects with metallic prosthesis or metallic cardiac pacemakers.¹⁸ In the meantime, optical techniques have advantages such as offering quantitative information and the possibility of repeated and prolonged measurements. Thus, the optical techniques have the potential to deepen our understanding of female sexual dysfunction and FSAR. However, to the best of our knowledge, there is no article that rigorously summarizes the studies of the use of optical techniques in FSAR assessment. To fill out the gap, this review article aims to summarize previous studies of FSAR assessment during sexual stimulation via either electrical nerve stimulation (preclinical animal models), drug administration (preclinical animal models), and visual stimulation (human subjects), solely or as a combination using optical techniques. We believe that this work can offer an overview of the current status of the field and draw the attention of the professionals, including researchers, biomedical engineers, and optical engineers, in the relevant fields for further advancement of female sexual dysfunction monitoring and treatment and understanding of FSAR in the future. Meanwhile, clinicians who are interested in involving or understanding such technologies for their clinical studies may also benefit from this work.

Methods

Using search engines PubMed, Google Scholar, and MEDLINE, articles were retrieved using the terms “female sexual dysfunction, female sexual arousal response, LDF, PPG, NIRS” from 1974 to 2024. After screening for relevance (ie, whether works that performed experiments using optical techniques rather than discussing the potential of using optical techniques), removing duplicates, and the language of the articles, 18 articles were selected for review. 18 articles include 11 articles that used LDF, four articles that used PPG, and three articles that used NIRS to study FSAR. In this review article, we aimed to cover various optical techniques used to evaluate FSAR, including both preclinical and clinical studies. While the review does not cover all of the previous works relevant to the use of optical techniques in female sexual studies, we endeavored to include all available techniques and present current applications of the techniques. Thus, this article can be a narrative mini-review for clinicians and researchers in the fields of sexual health, biomedical engineering, and optical technology who are interested in using optical techniques to investigate female sexual responses.

Optical techniques used in monitoring female sexual arousal response

Experiments in animals

Laser Doppler flowmetry.

Laser Doppler flowmetry is one of the most commonly used optical techniques to investigate FSAR among various optical techniques. As the name implies, LDF utilizes the Doppler shift (frequency change) of the illuminated laser light to acquire relative changes in blood flow perfusion. More specifically, the illuminated laser light undergoes scattering, which results in Doppler shifts due to the movement of red blood cells. Then, a portion of the backscattered light is detected using an optical detector. Finally, frequency analysis of the detected light amplitude offers us relative blood flow information.^{19,20}

Up to now, LDF has been utilized to investigate various aspects of FSAR in preclinical studies, such as exploration of new treatments for female sexual dysfunction, interrogation of new sexual stimulation approaches, and expansion of our understanding regarding female sexual arousal and female sexual dysfunction.

Some groups used rodents to investigate the influence of nerve stimulation using LDF. In a study by Vachon et al., the feasibility of using female Sprague-Dawley (SD) rats as models to study female sexual stimulation was investigated. The researchers monitored clitoral and vaginal blood flow using LDF during dorsal clitoral and plexus nerve stimulation (pulse duration: 0.2 ms, frequency: 20 Hz, duration: 5 s; amplitude not specified). By observing the increase of clitoral and vaginal blood flow during the stimulation, the authors confirmed that the female SD rat could be used to study FSAR.²¹ Giuliano et al. comprehensively investigated qualitative physiological changes caused by sexual arousal in female SD rats.²² Ovariectomy (OVX) rats were used to minimize the influence of hormones in the study. Using a microprobe, vaginal wall or intracavernosal blood flow, partial oxygen tension, temperature, and vaginal contractile activity were evaluated during stimulation of either paravaginal nerve, pelvic nerve, and paravertebral sympathetic chain (amplitude: 6 V, pulse duration: 1 ms, frequency: 10 Hz, for 30 s), and pelvic nerve and paravertebral sympathetic chain serially (amplitude: 6 V, pulse duration: 1 ms, frequency: 10 Hz, pelvic nerve stimulation for 90 s and paravertebral sympathetic chain for 30 s after 30 s of the pelvic nerve stimulation). The study showed that perfusion measurement allows reliable evaluation of vaginal blood engorgement. In addition, this study suggested that acetylcholine may play a critical role in the contraction phase induced by pelvic nerve stimulation while its influence in increasing vaginal blood engorgement is not significant.

While the above-mentioned studies used nerve stimulation with a fixed frequency, there have been studies that investigated blood flow changes caused by nerve stimulation with different stimulation frequencies using LDF. Rice et al. performed short-duration and long-duration (amplitudes: 0.5–3 V (most stimulation used 2 V), pulse durations: unknown (varying durations), frequencies: 1–100 Hz (most stimulation used 10 Hz), for 0.15–60 min) pudendal nerve stimulations on female SD rats to analyze time-frequency components of vaginal blood flow perfusion signals.²³ The authors tried to study various frequency components, mainly low-frequency components, of LDF blood flow signals, including neurogenic (0.076–0.200 Hz) and myogenic (0.200–0.740 Hz) frequency bands using continuous wavelet transform (CWT). This study represented that repeated or elongated stimulation can keep increasing blood flow in the vagina. Besides, based on raw blood flow signals, and neurogenic and myogenic components of the blood flow signals, the authors claimed pudendal modulation might potentially be used for treating female sexual dysfunction via enhancing genital arousal. Notably, the authors performed experiments with rats in different estrous cycles concerning the influence of the cycles on the experimental results. However, blood flow data from animals in different cycles did not show a statistically significant difference between each other, even though animals from different cycles showed different trends in vaginal blood flow changes. A female SD rat study by Zimmerman et al. also tested various frequencies to understand the mechanism of

tibial nerve stimulation (amplitude: unknown, pulse duration: 0.2 ms, frequencies: 10–25 Hz, for either 30 min continuously or 1-min stimulation followed by 1-min rest for a total time of 30 min) by measuring the vaginal blood flow using LDF.²⁴ Like the study by Rice et al., this study also utilized CWT to analyze the vaginal blood flow signals further. Among various frequency bands, the authors focused on examining the neurogenic bands. In this exploratory study, stimulation with different frequencies did not cause any significant difference in the neurogenic band of the vaginal blood flow signals. Meanwhile, the study proved that tibial nerve stimulation could be an alternative approach for inducing sexual arousal by increasing the vaginal blood flow and its energy of the neurogenic frequency band.

A study by Park et al. used rabbits to investigate the influence of nerve stimulation using LDF.²⁵ Park et al. examined vasculogenic female sexual dysfunction using an atherosclerotic model of New Zealand white female rabbits. The atherosclerotic model was developed by feeding a 0.5% cholesterol diet and inducing an injury at the common and external iliac arteries in the rabbits. After 16 weeks of the diet, pelvic nerve stimulation (amplitude: 10 V, pulse duration: 8 ms, frequency: 16 Hz, for 20 s) was performed on the rabbits. Using LDF, the authors showed that atherosclerotic animals have less vaginal and clitoral blood flow before and after the stimulation than one of the control groups. Besides, their finding from blood flow measurement was supported by additional information such as vaginal wall pressure measurement and histological examination. This study suggested that atherosclerosis may be associated with female sexual dysfunction, resulting in abnormal vaginal engorgement and clitoral erection.

Meanwhile, the other studies investigated the influence of pharmacological or chemical stimulation, combined with nerve stimulation, using LDF. Tarcan et al. performed pelvic nerve stimulation (amplitude: 10 V, pulse duration: 8 ms, frequency: 16 Hz, for 30 s) on New Zealand white female rabbits without and with apomorphine (APO), a type of dopamine agonist that has been tested to treat sexual dysfunction, administration varying doses (0.05, 0.1, 0.2, 0.3, and 0.4 mg/kg) in the rabbits.²⁶ Among various doses, 0.1 and 0.2 mg/kg concentration of APO combined with the nerve stimulation showed the maximum change of blood flow at the clitoris and vaginal wall. In another study, Adaikan et al. evaluated the effectiveness of phytoestrogens in a menopausal OVX model of New Zealand white rabbits using LDF.²⁷ After complete recovery from the OVX surgery, 24 animals were divided into four groups: water-administered control group; Estradiol valerate (human estrogen with the highest potent)-administered group (100 µg/kg dosage); daidzein (one of the natural isoflavones)-administered group (100 µg/kg dosage), and isoflavone phytoestrogen from red clover extract (6.68 mg/kg dosage, estimated to be equivalent to 100 µg/kg dosage of daidzein)-administered group. Animals in each group were orally administered the corresponding suspensions daily for 12 weeks. And blood flow was measured in the vagina using LDF before, during, and after pelvic nerve stimulation (amplitude: 10 V, pulse duration: 0.8 ms, frequency: 16 Hz, for 30 s). In the daidzein-administered group, the increase in blood flow was the highest. In the estradiol valerate-administered group, the uterine weight was remarkably increased, while the bone density was the highest in the red clover extract group. A

study by Angulo et al. interrogated the effect of vardenafil (1 mg/kg dosage), a phosphodiesterase type 5 (PDE5) inhibitor that was known to improve penile erection preclinically and clinically, for improving the clitoral and vaginal blood flow in mature female Beagle dogs during pelvic nerve stimulation (amplitude: 30 mA current, pulse duration: 1 ms, frequencies: 5, 10, and 20 Hz, for 1 min).²⁸ While this study did not delve into the frequency band of LDF signals, the study reported exciting findings: (1) the effects of vardenafil administration last for up to 80 min which shows the potential of its long therapeutic window; (2) administration of vardenafil elongates blood flow increase caused by the nerve stimulation in the vagina and clitoris compared to the control group; and (3) among 5, 10, and 20 Hz frequency stimulation, compared to the control groups, 5 Hz frequency stimulation combined with vardenafil administration increased the blood flow most in the vagina and clitoris. Overall, this dog model study showed the potential of vardenafil for enhancing female sexual response. In the meantime, Zhang et al. explored a new treatment for female sexual dysfunction using soy isoflavone, a food-derived phytoestrogen, using 12-month-old C57BL/6 mice as a menopausal model.²⁹ Compared to the control group, the peak of vaginal blood flow change induced by pelvic nerve stimulation (amplitude: 6 V, pulse duration: 0.8 ms, frequency: 10 Hz, for 30 s with 5-min rest) was remarkably improved in the soy isoflavone-treated groups regardless of dosage. Likewise, results of enzyme-linked immunosorbent assay and histological evaluation showed that soy isoflavone has a positive effect on female sexual dysfunction.

Near-infrared spectroscopy.

Near-infrared spectroscopy is an optical spectroscopic technique that can allow us to track chromophore information, such as different types of hemoglobin, lipid, and water, depending on the number of utilized wavelengths, relatively or absolutely, depending on the measurement scheme. Utilizing relatively low absorption and high scattering properties of biological tissue, NIRS can achieve non-invasive measurement of chromophore information from relatively deep tissue.

A New Zealand white rabbit study by Min et al. investigated the effect of sildenafil, a PDE5 inhibitor, to enhance the sexual response caused by pelvic nerve stimulation (amplitude: 10 V, pulse duration: 0.8 ms, frequencies: 4, 16, and 32 Hz, for 30 s).³⁰ This study utilized frequency-domain NIRS for the measurement of the oxygen saturation and concentration of oxygenated hemoglobin, deoxygenated hemoglobin, and total hemoglobin (which is usually considered as the summation of the concentrations of oxygenated hemoglobin and deoxygenated hemoglobin) of the vaginal, labial, and clitoral tissues and laser Doppler imaging (LDI), which uses raster scanning of LDF signals to acquire a 2D blood flow map of the external genitals, for the measurement of the blood flow of the clitoral tissue. Before administering sildenafil, higher stimulation frequency resulted in higher hemoglobin concentration and blood flow during the pelvic nerve stimulation. Regardless of the stimulation frequencies used, as the dose of sildenafil increased, oxygenated hemoglobin, total hemoglobin, and oxygen saturation increased. For 4 and 16 Hz stimulation frequencies, as the dose of sildenafil increased, deoxygenated hemoglobin decreased. For 32 Hz stimulation frequency, however, deoxygenated hemoglobin did not change for 5 and 10 nM

sildenafil, while deoxygenated hemoglobin dramatically increased when 50 nM sildenafil was administered. In the meantime, for 4 and 32 Hz stimulation frequencies, blood flow decreased as the dose of sildenafil increased. For 16 Hz stimulation frequency, 5 and 10 nM resulted in similar blood flow, while 50 nM sildenafil reduced blood flow, compared to 5 and 10 nM sildenafil administration.

A study by Jeong et al. investigated to develop a NIRS vaginal probe that can measure vaginal temperature as well.³¹ After the development of the probe, the study performed a pilot sexual stimulation test on SD rats by administering APO (80 µg/kg dose) to confirm that the probe is capable of monitoring FSAR. The study demonstrated that the probe could be used in future female sexual studies by showing an increase in hemoglobin concentration after administration of APO. Another study by Jeong et al. used the optical probe to monitor the differences in the hemodynamic and temperature response of the vagina during sexual arousal via APO administration (80 µg/kg) in SD rats while anesthetizing animals using two different anesthetic agents: isoflurane and ketamine.³² This study showed the opposite trends of both oxygenated hemoglobin and total hemoglobin between isoflurane- and ketamine-anesthetized animals. Specifically, isoflurane-anesthetized animals showed a decrease in the relative concentration of oxygenated hemoglobin and total hemoglobin, which may indicate the reduction of vaginal perfusion. In contrast, ketamine-anesthetized animals showed an increase in the relative concentration of oxygenated hemoglobin and total hemoglobin, which may indicate an increase of vaginal perfusion. This study showed that the choice of anesthetic agents is critically important, and the characteristics of different anesthetic agents should be understood because different anesthetic agents in animal studies can result in different hemodynamic responses for the same sexual arousal.

Experiments in women

Laser Doppler flowmetry

Apart from preclinical studies, LDF has been utilized in clinical studies. To directly measure FSAR in women, Waxman et al. utilized LDI.³³ With their system, the image acquisition time of an image with 256×128 pixels was 2 min 43 s, which could capture about five images per 15 min. During image acquisition, healthy women (65 healthy women with a range of ages between 18 and 29 years old) first watched two non-sexual films, one film for adaptation of the subjects to the environment and another film for LDI baseline measurement. Then, among four films (one female-oriented sexual film and three non-sexual [one neutral, one humorous, and one anxiety control] films), a randomly assigned film was displayed to the subjects. The length of every film was 15 min. Subjects who watched a non-sexual film did not present significant blood flow variation in the external genitals compared to the baseline blood flow. Meanwhile, subjects who watched an erotic film presented a huge increase in blood flow in the external genitals compared to the baseline blood flow. Based on the experimental results and several advantages of LDI, including no requirement for probe contact and no insertion of the probe, the authors claimed that LDI could be a valuable tool for evaluating female sexual response. Still, the authors also mentioned that LDI has several disadvantages, such as high vulnerability to movement, slow image acquisition speed, and high cost of the commercial system (eg, >60 000 USD)

that should be addressed in the future for wide application of the technique. Another LDI study performed by Boyer et al.³⁴ aimed to push forward their previous study by Waxman and Pukall.³³ Boyer et al. explored criteria determining genital responsiveness and non-responsiveness for LDI and tested the applicability of LDI for investigating multiple sexual stimuli within a single test. Among 43 heterosexual women screened, 28 women finished all of the study protocols. Some of the measurement data were excluded due to various reasons, such as technical issues and pigmentation of the tissue. Compared to their previous study, the team modified the experimental protocols. Specifically, adaptation and baseline measurement time was decreased from 15 to 8 min, visual sexual stimulation time was reduced from 15 to 7 min (a sexual video of the same mixed couple played for 4 min and a video of either oral sex performed on female or male–female intercourse for 3 min), and addition of 15 min. In the end, a 14-min length nature film was shown to the subjects so that the blood flow could return to the baseline. The study successfully demonstrated that LDI could be used to investigate multi-session sexual stimuli by showing a return of the LDI blood flow to 5%–10% of the baseline within 9–10 min after watching an erotic film. However, the authors described that exploration of predictors of genital non-response could not be achieved due to the limited sample size and demographic characteristics.

Laser Doppler flowmetry is the most frequently used optical technique in FSAR studies. Thus, we have a relatively good understanding of how blood flow changes during FSAR caused by different sexual stimulations. However, due to the relatively high price of commercial LDF systems, LDF systems cannot always be the first option. Considering this point, more comparison studies using LDF with PPG and NIRS, which are usually cheaper than LDF, can be performed so that we can know how different physiological parameters collected using PPG and NIRS change as blood flow is measured using LDF changes.

Photoplethysmography

Photoplethysmography is an optical tool used to detect blood volume changes and pressure pulses. For studying female sexual arousal response, two types of PPG have been introduced, including vaginal PPG and labial PPG.^{35–38} The tools have been utilized in various studies, ranging from simple evaluation of female sexual arousal to comparison of sexual response when different types of sexual stimulation are given.

Some studies observed the influence of watching different types of videos as visual stimulation. A study by Geer et al. introduced PPG for vaginal measurement, which was one of the first studies introducing vaginal PPG.³⁵ Twenty undergraduate female students participated in the study. This early study showed that the vaginal blood volume and pressure pulse increased when subjects were shown an erotic film, compared to the ones in the resting state and the ones when subjects were shown a non-erotic film. Interestingly, vaginal PPG measurement and subjective evaluation of the degree of sexual arousal using a questionnaire were not correlated with each other. The authors postulated that this conflict may be due to low and moderate visual stimulation levels rather than a strong level of visual stimulation.

Meanwhile, Prause et al. performed a study to compare vaginal PPG and labial PPG measurements.³⁶ Fifteen female subjects (age: 18–21 years old, mean: 19.8 years old,

standard deviation: 0.9 years old) participated in the study. Experimental protocols consist of three 3-min videos: a 3-min video of consensual intercourse (1 min of foreplay, 1 min of oral sex, and 1 min of penile-vaginal intercourse), a 3-min anxiety-inducing video, and a 3-min sound of forced heterosexual intercourse without displaying the corresponding video. During the experiments, vaginal PPG was inserted into the vagina of the subjects, while labial PPG was placed on one of the labia minora of the subjects. This study suggested that labial PPG can be a potential tool that can substitute vaginal PPG by presenting similar experimental results and less disturbance to subjects compared to vaginal PPG. Bouchard et al. performed an interesting study that monitored the vulvar blood flow using LDI and the vaginal blood volume using vaginal PPG during visual stimulation.³⁷ Thirty-one subjects (age: 18–30 years old) participated in the study. Visual stimulation protocols included a 6-min nature video for adaptation, a 9-min nature video for baseline measurement, six 3-min videos of foreplay, another 9-min nature video for rebounding to the baseline, and six 3-min videos showing penile–vaginal intercourse. This study included two different types of visual stimulation (eg, foreplay and intercourse) to investigate whether or not these visual stimulations would result in different stimulation outcomes. It is noteworthy that the laser source of LDI was causing unwanted interference in vaginal PPG measurement significantly increasing the amplitude of the measurement. Thus, the authors did not use interfered vaginal PPG signals for analysis. One interesting finding of the study was that foreplay and intercourse videos caused a similar degree of sexual response. Also, the study showed that the vulvar response was significantly more correlated with a subjective answer to a questionnaire for sexual arousal than the vaginal response. Studies of Geer et al.³⁵ and Bouchard et al.³⁷ showed that vaginal response was not strongly correlated with the answers for the subjective evaluation of the participants. However, it should be noted that the answers to the questionnaire cannot perfectly reflect FSAR during the stimulation.

Not like studies of Geer et al. and Bouchard et al., Henson et al. attempted to compare the vaginal and labial response to visual stimulation and tactile stimulation using vaginal PPG and a thermistor to monitor labial temperature as an indicator of the labial blood volume.³⁸ Five subjects participated in this study. Visual and tactile stimulation studies were performed separately, with more than one month between the two studies. The visual stimulation study involved displaying an ~11-min-long erotic film while subjects were asked to perform manual manipulation of the genitalia in the tactile stimulation study. Before reaching orgasm, the sexual response of the vaginal and labial blood volume did not show a significant difference while both were increasing primarily for different types of stimulation. However, when subjects reached orgasm during manual stimulation, the vaginal and labial blood volumes were strongly negatively correlated, which did not happen in visual stimulation.

While PPG cannot provide blood flow information like LDF, PPG can still provide information on blood volume that is necessary to investigate the engorgement of female genitalia. Since PPG is relatively simple and low cost, it can be considered for studying the FSAR of females in underdeveloped countries. As Bouchard et al. did, multi-modal measurement with LDI or LDF can also be considered to get additional information about FSAR.

Compared to LDF and PPG, NIRS is a relatively new technique in FSAR studies. Thus, only limited studies were performed using NIRS. Because NIRS can provide other or more information than that of LDF or PPG, respectively, multi-modal studies incorporating LDF could be performed to better understand the interplay of different hemodynamic parameters (blood flow and oxygenation) during FSAR.

Discussions and future perspectives

A summary of the optical techniques to monitor FSAR is provided in Table 1. As described, optical techniques, including LDF, PPG, and NIRS, have been utilized to expand our knowledge about FSAR. Advantages such as low cost, non-invasiveness, and offering quantitative information can potentially make optical techniques popular tools in FSAR assessment. Table 2 shows the characteristics of each optical technique. Although existing optical techniques have been successfully used in various types of FSAR assessment, there is still room for improvement in the investigation of FSAR, which will be investigated in the future.

First, non-human primate models can be considered in future studies. While non-human primates were used in FSAR studies,³⁹ no study used optical techniques to investigate FSAR in non-human primate models. Preclinical studies covered in this work are limited to using small animals such as rodents, rabbits, and dogs. Like other preclinical studies, sometimes preclinical FSAR studies show discrepancies from relevant clinical FSAR studies. This may be partially caused by physiological differences between humans and small animals used in optical techniques-based previous FSAR studies. Studies with non-human primate models will be able to provide insights that can be more readily translated into clinical practices since non-human primate models will likely have similar physiological characteristics to humans.

Second, the influence of different anesthetics on FSAR assessment should be seriously investigated. As demonstrated by Jeong et al.,³² for the same sexual stimulation, animals showed different physiological responses as different anesthetics were used for anesthesia. For example, while a thorough comparison of different anesthetics should be performed, propofol could be avoided, or an artificial ventilator should be used together during an FSAR study using propofol-anesthetized animals due to the suppression of breathing.⁴⁰ This partially shows that anesthetics is another factor that can lead to discrepancies between studies from different groups and between preclinical and clinical studies. Thus, studies that investigate the effects of anesthetics on FSAR during various stimulation schemes should be urgently performed. In the meantime, optical monitoring approaches that do not require anesthesia and cause much stress on preclinical animal models can be investigated as alternative approaches.

Third, standardized protocols can be developed in pre-clinical studies to better understand the differences between species and generalize the experimental outcomes. For example, even though a myriad of LDF FSAR studies were performed, it is hard to generalize the outcomes and compare the outcomes from different species due to the use of different experimental protocols, including the placement of LDF probes. It is expected that experiments with standardized protocols will allow us to interpret and compare experimental results from different studies more easily.

Table 1. Summary of evaluation of female sexual arousal response (FSAR) with optical techniques.

Type	Measurement	Stimulation	Experimental subjects	Optical technique	Key findings	Ref.
Pre-clinical (animal) studies	Blood flow	Dorsal clitoral and pelvic plexus nerves	SD rats	LDF	Observed increased clitoral and vaginal blood flow during dorsal clitoral and pelvic plexus nerves.	21
	Blood flow, partial oxygen tension, temperature, and vaginal contractile	Paravaginal and pelvic nerves	SD rats (OVX)	LDF	Identified acetylcholine's role in vaginal contractions during pelvic nerve stimulation.	22
	Blood flow	Pudendal nerve	SD rats	LDF	Studied frequency components (eg, neurogenic, myogenic) of LDF signals; estrous cycle effects are minimal.	23
	Blood flow	Tibial nerve	SD rats	LDF	Proved tibial nerve stimulation as an alternative for inducing sexual arousal.	24
	Blood flow	Pelvic nerve	New Zealand white rabbits	LDF	Demonstrated reduced blood flow in atherosclerotic models linked to vasculogenic FSD.	25
	Blood flow	Pelvic nerve and APO	New Zealand white rabbits	LDF	Apomorphine (APO) enhanced blood flow, with optimal response at 0.1-0.2 mg/kg.	26
	Blood flow	Pelvic nerve	New Zealand white rabbits (OVX)	LDF	Phytoestrogens increased vaginal blood flow, daidzein showing the highest response.	27
	Blood flow	Pelvic nerve and vardenafil	Beagle dogs	LDF	Vardenafil enhanced clitoral and vaginal blood flow, with optimal responses at 5 Hz frequency.	28
	Blood flow	Pelvic nerve	C57BL/6 mice	LDF	Soy isoflavone improved FSAR, supported by histological evaluations.	29
	Blood flow and hemoglobin concentration	Pelvic nerve and sildenafil	New Zealand white rabbits	NIRS and LDI	Sildenafil improved FSAR via increased oxygenation metrics with frequency-dependent responses.	30
	Hemoglobin concentration and temperature	APO	SD rats	NIRS	Increased hemoglobin concentration was observed during FSAR using NIRS.	31
	Hemoglobin concentration and temperature	APO	SD rats	NIRS	Highlighted anesthetics' influence on hemodynamic responses during FSAR monitoring.	32
	Blood flow	Visual	Human subjects	LDF	Demonstrated LDI as a non-invasive method for assessing FSAR with significant blood flow increases.	33
	Blood flow	Visual	Human subjects	LDF	Showed LDI's potential for multi-session FSAR testing with quick blood flow recovery times.	34
Clinical studies	Blood volume and pressure pulse	Visual	Human subjects	PPG	Explored FSAR dynamics using LDF, advancing understanding of arousal responses.	35
	Blood volume and pressure pulse	Visual	Human subjects	PPG	Studied long-term effects of stimulation on FSAR-related blood flow dynamics.	36
	Blood flow and blood volume	Visual	Human subjects	PPG	The vulvar blood flow response (LDI) correlated more significantly with subjective sexual arousal than the vaginal response. Foreplay and intercourse videos caused similar sexual responses.	37
	Blood volume and pressure pulse	Visual and tactile	Human subjects	PPG	Highlighted the role of tibial nerve modulation in enhancing FSAR.	38

Abbreviations: APO, apomorphine; LDF, laser Doppler flowmetry; LDI, laser Doppler imaging; NIRS, near-infrared spectroscopy; PPG, photoplethysmography; OVX, ovariectomy; SD: Sprague–Dawley.

Fourth, more clinically relevant animal models or experimental protocols should be developed to understand the underlying mechanisms of female sexual arousal thoroughly. While human sexual arousal is the combination of central and genital arousal,⁴¹ animal studies tend to focus on genital arousal, which is only a part of the process. Thus, more attention should be paid in animal experiments to ensure more

translatable results for clinical studies. Meanwhile, both the brain and genitalia should be monitored,^{41,42} considering that FSAR is a complicated process that involves both the brain and genitalia.

Last but not least, more clinical studies should be performed. While these techniques can show various physiological responses during FSAR, limited clinical studies have

Table 2. Characteristics of each optical technique.

Technique	Advantages	Disadvantages	Best practices
LDF	• Can measure superficial blood flow perfusion. • Non-contact blood flow measurement is possible (in the case of LDI).	• Deep blood flow cannot be measured. • Highly sensitive to motion artifacts. • Highly sensitive to probe positioning (should be positioned on the top of a blood vessel).	• Can be used for real-time measurements of superficial blood flow. • Motion artifacts should be minimized by stabilizing the target area.
PPG	• Relatively simple system. • Can measure the blood volume and pulse relevant to the engorgement of the genitalia.	• May lack sensitivity for detecting subtle physiological changes. • Limited depth penetration.	• Best for measurement in resource-limited settings.
NIRS	• Allows exploration of physiological mechanisms at deeper tissue depths by changing the source-detector separation. • Can measure relative (with continuous-wave source) and absolute change (with amplitude-modulated source) of blood volume, hemoglobin concentrations (oxygenated hemoglobin, deoxygenated hemoglobin, and total hemoglobin), and blood oxygenation	• Requires more complex experimental setups (with amplitude-modulated source). • Due to the measurement of diffusely back-reflected light, signals come from a volume of the tissue.	• Can be used for studies requiring deeper penetration depth and tissue oxygenation measurement. • Multiple source-detector pairs can be considered for depth-resolved measurements.

Abbreviations: LDF, laser Doppler flowmetry; LDI, laser Doppler imaging; NIRS, near-infrared spectroscopy; PPG, photoplethysmography.

been performed. The limited number of clinical studies is the most critical factor preventing the use of optical techniques in clinical routines. Especially, clinical studies involving NIRS or tissue oximetry, solely or with different modalities, may need to be performed by different groups to test the effectiveness of NIRS and provide more information about female sexual arousal. If multiple clinical studies are performed and the robustness of the techniques in clinical FSAR studies is proven, the optical techniques can go through the processes of medical device approvals and clearances.

In terms of technical development, several things can be considered. First, non-contact systems can be developed in the future. Except for LDI, all the optical techniques used for the FSAR study required the attachment of the system to the region of interest. While studies that require the measurement vaginal wall should use contact systems, other types of studies can be performed using non-contact systems as well. The use of non-contact systems will reduce the feeling of discomfort, so that the data collected from the participants of the experiments can be more realistic than that acquired using contact systems. Second, optical techniques other than LDF, PPG, and NIRS can be potentially considered for use in FSAR assessment in the future. While LDF, PPG, and NIRS have several advantages in FSAR assessment, the information from such techniques is still limited. Some optical techniques can potentially be used in FSAR assessment with slight modification. Recently, endoscopic-type optical coherence tomography (OCT)⁴³ and photoacoustic endoscopy (PAE)⁴⁴ have been introduced to investigate vaginal tissue characterization. By being sensitive to refractive index differences, OCT can visualize 3D images of the tissue investigated. PAE can visualize 3D images of chromophores depending on the wavelengths used. If the imaging speed of OCT and PAE can be fast enough, OCT and PAE can be used to visualize 3D images of the variation

of the vaginal tissue anatomically and chromophores of the vaginal tissue during sexual stimulation or drug administration, respectively. Raman spectroscopy is another potential optical technique that can be utilized to investigate FSAR since Raman spectroscopy is sensitive to the chemical changes of the vaginal fluid.⁴⁵ Multi-modal systems combining multiple techniques and acquiring various information during stimulation or drug administration can also be considered to understand FSAR and female sexual dysfunction more systematically.

Conclusion

In this work, we introduced research that utilized optical techniques (LDF, PPG, and NIRS) to evaluate FSAR during various interventions in both preclinical and clinical studies. We also overviewed the limitations and possible future research directions of the field. These techniques have demonstrated significant potential in preclinical and clinical studies due to their non-invasive nature, cost-effectiveness, and ability to provide quantitative information. As such, they are positioned as valuable tools for advancing both research and clinical applications related to FSAR and female sexual dysfunction. This review will serve as an overview for researchers and clinicians in the fields of sexual health, biomedical engineering, and optical technology. For researchers, the review may provide a comprehensive summary of the optical techniques employed in FSAR studies, offering insights into their methodologies, benefits, and limitations. We hope that more researchers will be involved in addressing these gaps, such as exploring the effects of different anesthetics in FSAR studies and developing more practical tools. For clinicians, this review may provide an overview of the optical technologies for researching FSAR, so that they can consider using appropriate techniques in

various conditions and subjects for quantitative analysis of the clinical investigations. We believe that this work will be able to elaborate on more exciting and important research works so that more advanced approaches can be explored to treat female sexual dysfunction and widen our understanding of FSAR in the future.

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Author contributions

H.J.: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Writing—original draft, writing—review & editing. M.S.: Data curation, Formal analysis, Investigation, Funding acquisition, Methodology, Validation, Writing—original draft, writing—review & editing. K.P.: Conceptualization, Writing—review & editing, Supervision. J.G.K.: Conceptualization, Funding acquisition, Methodology, Validation, Writing—review & editing, Supervision.

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Conflicts of interest

The authors declare that they have no competing interests.

Data availability

All the data and the materials are presented in the manuscript.

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