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**TRABALHO FINAL**
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# Neurophysiological bases of erogenous sensitivity: A special focus on women's breast

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**ABSTRACT:**

This work delves into the intricate world of erogenous sensation, a complex phenomenon that plays a pivotal role in sexual arousal and pleasure. Drawing from a wealth of research in both animal studies and human neuroimaging, the neurophysiological underpinnings of erogenous sensation are elucidated, with a specific focus on the breast as a crucial erogenous zone for women. The term "erogenous sensation" is introduced to encapsulate the sensitivity of specific body areas to touch and stimulation, shedding light on its importance in understanding sexual behaviour, intimate experiences, and overall well-being.

Through a comprehensive review of literature, the work explores the neural pathways involved in processing genital touch, the cortical representation of erogenous zones, and the interconnectedness of tactile and visual stimulation in sexual interactions. Furthermore, the impact of erogenous sensation on sexual dysfunction, quality of life, and medical impairments caused by various clinical conditions is discussed, emphasizing the need for further research in this understudied area.

The preservation of breast sensibility emerges as a critical objective in surgeries, with a focus on techniques to restore sensation in breast cancer patients undergoing reconstruction. Insights from studies on breast surgery highlight the importance of meticulous surgical planning to retain erogenous sensation and enhance overall quality of life.

In conclusion, this work advocates for a deeper understanding of erogenous sensation and its implications for sexual well-being. By acknowledging the significance of erogenous sensitivity, particularly in women, and exploring avenues to enhance sexual experiences, it aims to contribute to a broader knowledge of human sexuality and relationships, paving the way for potential interventions to address sexual dysfunctions and improve overall quality of life.

**KEY WORDS:** erogenous sensation, sexual arousal, breast, mammaplasty

**Trabalho Final de Mestrado**

Catarina Mota Araújo

Este trabalho explora o mundo da sensibilidade erógena, um fenômeno complexo que desempenha um papel fundamental na excitação sexual e no prazer. Com base em vários estudos em animais e imagiologia humana, são elucidadas as bases neurofisiológicas da sensibilidade erógena, com um foco específico na mama como uma zona erótica crucial para as mulheres. O termo "sensibilidade erógena" é introduzido para encapsular a sensibilidade de áreas específicas do corpo ao toque e à estimulação, enfatizando a sua importância na compreensão do comportamento sexual, das experiências íntimas e do bem-estar geral.

Por meio de uma revisão abrangente de literatura, o trabalho explora as vias neurais envolvidas no processamento do toque genital, a representação cortical das zonas erógenas e a interconexão da estimulação tátil e visual nas interações sexuais. Além disso, são discutidos os impactos da sensibilidade erógena na disfunção sexual, na qualidade de vida e nos prejuízos médicos causados por diversas condições clínicas, destacando a necessidade de mais pesquisas nesta área pouco estudada.

A preservação da sensibilidade mamária surge como um objetivo crítico em cirurgias, com foco em técnicas para restaurar a sensibilidade em pacientes com cancro da mama submetidos a reconstrução. “Insights” de estudos sobre mamoplastia e reconstrução mamária destacam a importância de um planeamento cirúrgico meticuloso para manter a sensibilidade erógena e melhorar a qualidade de vida geral.

Em conclusão, este trabalho defende uma compreensão mais profunda da sensibilidade erógena e suas implicações para o bem-estar sexual. Ao reconhecer a importância desta sensibilidade, especialmente nas mulheres, e explorar maneiras de aprimorar as experiências sexuais, este trabalho visa contribuir para um conhecimento mais amplo da sexualidade humana e dos relacionamentos, abrindo caminho para possíveis intervenções para tratar disfunções sexuais e melhorar a qualidade de vida geral.

**PALAVRAS-CHAVE:** sensação erógena, excitação sexual, mama, reconstrução mamária

**RESUMO:**

O sexo é fundamental para a sobrevivência da espécie humana e, neste trabalho, decidiu introduzir-se o termo "sensibilidade erógena" para definir o fenômeno caracterizado pela sensibilidade de áreas específicas do corpo ao toque e à estimulação, que provocam sentimentos de prazer e excitação sexual. A perceção da sensibilidade erógena é uma interação complexa entre o sistema nervoso central e periférico, abrangendo diferentes regiões cerebrais e recetores especializados, que influenciam profundamente o comportamento sexual e as experiências íntimas.

Estudos em animais e humanos, revelaram que tanto centros do tronco cerebral como do hipotálamo participam no processamento desta sensibilidade e que, as fibras tácteis-C, responsivas ao toque suave e associadas à liberação de oxitocina, influenciam a perceção de estímulos sexuais, embora a sua presença na pele dos órgãos genitais ainda permaneça incerta. Para além disso, diferentes investigações demostraram que o canal iónico mecanossensível PIEZO2 é também importante na sensibilidade genital e função sexual e que, com a ativação destes recetores, se desencadeiam respostas prazerosas. Indivíduos com uma perda de função bialélica do PIEZO2 têm então uma diminuição significativa da sua sensibilidade erógena genital.

Em 1966, Masters e Johnson propuseram um modelo para explicar o ciclo de resposta sexual humana composto por quatro fases: excitação, "plateau", orgasmo e resolução. Este foi mais tarde criticado por Kaplan em 1974, que propôs um novo modelo trifásico: desejo, excitação e orgasmo. Aqui, fatores psicológicos como a motivação e a atenção, passaram a ser tomados em conta. Atualmente, segue-se o modelo apresentado nos manuais DSM que mistura ambos os modelos apresentados, e define então quatro fases do ciclo sendo estas o desejo, excitação, orgasmo e resolução. Este modelo é bastante útil para a análise da disfunção sexual, já que esta está relacionada com alterações em uma ou mais fases deste ciclo de resposta. A disfunção sexual apresenta desafios significativos, que afetam a qualidade de vida das pessoas e, por isso, a descoberta de curas ou técnicas para experienciar novas formas de prazer é crucial nestes doentes.

A sensibilidade erógena, como mencionada previamente, pode ser desencadeada pelo toque de diversas partes do corpo, conhecidas como zonas erógenas. Na mulher, para além da já conhecida zona genital, temos também zonas erógenas extra-genitais como a mama, lábios, pescoço e interior da coxa, que podem induzir o orgasmo quando

estimuladas. Estudos mostram que 95,3% das mulheres sentem prazer quando estimuladas em áreas não-genitais e 12% conseguem alcançar o orgasmo quando o peito é estimulado. Assim, preliminares e estimulação de zonas diferentes do corpo feminino são cruciais para a vida sexual da mulher e a falta delas é uma queixa comum. A sensibilidade é algo que varia entre as diferentes áreas do corpo tendo-se verificado em investigações que o clitóris é a zona mais sensível à vibração, enquanto que na mama a zona de maior sensibilidade é o mamilo. Entender estas diversas sensibilidades é fundamental para uma promoção eficaz da excitação sexual.

Explorando em mais detalhe a mama feminina, a sua estimulação é uma prática ancestral e promotora de emoções positivas e intimidade sexual. A oxitocina, também conhecida como a hormona do amor, é liberada durante a amamentação, excitação sexual e orgasmo, contribuindo para o vínculo do casal e para a redução de stress.

Estudos sobre a anatomia, histologia e inervação mamária são essenciais para a melhor compreensão desta zona, visando preservar a sensibilidade erógena da mama aquando uma cirurgia de redução ou reconstrutiva. Anatomicamente, a glândula mamária desenvolve-se desde a fase embrionária até à vida adulta sendo que, durante a gravidez, existem mudanças hormonais e morfológicas que preparam a mulher para amamentar. Já na menopausa e no tempo que se segue, ocorre uma involução hormonal, substituindo-se o tecido glandular da mama por tecido adiposo. Em termos histológicos a mama é um complexo arranjo de lobos, ductos e tecido conjuntivo, sendo que em cada mamilo "descarregam" nove lobos e ductos. O estudo da fáscia peitoral em si é importante na cirurgia mamária uma vez que, a prega inframamária é uma zona de incisão. Passando à vascularização, esta possui variabilidade entre indivíduos, mas elementos consistentes incluem a artéria torácica interna, artéria torácica lateral, artéria toracoacromial e ramos terminais das perfurantes das artérias intercostais (da terceira à oitava). Já a drenagem venosa principal é feita pela veia axilar, que se transforma na subclávia ao passar pela clavícula. Em destaque temos também o plexo venoso subareolar, que drena superficial ou profundamente. Por último, a inervação da mama é feita por ramos anteriores e laterais cutâneos do segundo ao sexto nervos intercostais tendo o quarto nervo um destaque importante. Para além disso, a inervação da mama e da pele que a recobre estão interligadas pelo facto de partilharem a mesma origem ectodérmica.

O complexo formado pelo mamilo e auréola é a zona mais sensível da mama como já referido anteriormente. Assim, o seu estudo é também relevante pelo papel que desempenha na sensibilidade erógena da mulher.

Como última análise, este trabalho foca-se também em duas cirurgias mamárias, a redução e a reconstrução. A cirurgia de redução é a sétima operação mais realizada e, de facto, as mulheres que se submetem a este procedimento pretendem não só um melhor aspeto visual, mas também um alívio sintomático (dor de costas, entre outros) devido à sua hipertrofia mamária. Várias técnicas para a redução cirúrgica foram estudadas e atualmente existem duas que são mais utilizadas não havendo, no entanto, investigações suficientes que possam de facto escolher uma em detrimento da outra. Sabe-se sim que esta cirurgia traz, para além de mais conforto para a mulher, uma melhor sensibilidade erógena à que apresentava previamente pela redução de volume. Já em termos reconstrutivos, o cancro da mama é uma patologia mundialmente conhecida e que afeta inúmeras mulheres levando muitas vezes à necessidade de realização de mastectomia. A mastectomia, por sua vez, é um procedimento bastante mais complexo para os cirurgiões e que, mais facilmente, afeta a sensibilidade da mama. A queixa de falta de sensibilidade pós-cirúrgica é uma queixa frequente nesta população. A reconstrução autóloga, ou seja, com recurso a um retalho de tecido de outra zona do corpo, mais frequentemente do abdómen, é uma abordagem utilizada até em conjunção com a colocação de implante. Sabe-se então, por meio de artigos, que o uso de retalhos inervados traz benefícios sensitivos para a mama reconstruída.

Em termos de conclusão, este trabalho prende-se com o intuito de demonstrar a necessidade do estudo da sensibilidade erógena da mulher para a sua saúde sexual e, assim, promovendo o bem-estar geral. Ter uma visão personalizada de cada pessoa e de que zonas são mais prazerosas quando estimuladas sendo a mama a zona extra-genital erógena mais mencionada. Procurar estratégias para uma possível melhoria de tratamento de disfunções sexuais. E por último, perceber de que maneira a cirurgia mamária pode ser realizada pelos cirurgiões de modo a preservar a sensibilidade erógena que é, para a mulher, um fator igualmente importante à aparência exterior.

**TABLE OF CONTENTS:**

**GLOSSARY:**

**CT –** C-tactile

**DIEP –** deep inferior epigastric artery perforator

**FSAD –** female sexual arousal disorder

**IP –** inferior pedicle

**ms-TRAM –** muscle-sparing transverse rectus abdominis myocutaneous

**NAC –** nipple-areola complex

**NE –** nipple erection

**NO –** nitric oxide

**NOS –** nitric oxide synthase

**PAG –** periaqueductal grey matter

**SCI –** spinal cord injury

**SMP –** superomedial pedicle

**TRAM –** transverse rectus abdominis myocutaneous

## 1. INTRODUCTION:

Sex is fundamental to the survival of our species and can be both pleasurable and frustrating, because of unsatisfying experiences or inadequate performance. The reason why approaching this theme is important is because sex is clearly more complex than mere reproduction and it influences people's well-being. Like other forms of learning, sexual behaviour develops over time when people learn which stimuli arouses them more (body features, personality, contextual cues, etc.). (Pfaus et al., 2012)

Despite the extensive literature on sexual arousal, a specific term to describe the type of touch that triggers such responses has been lacking. To address this gap, the concept of "erogenous sensation" is introduced in this work. Erogenous sensation can be viewed as a complex phenomenon characterized by the sensitivity of specific body areas to touch and stimulation, which evoke feelings of sexual arousal and pleasure. (Nummenmaa et al., 2016; Younis et al., 2016)

Understanding the intricate interplay between the peripheral and central nervous systems, and sexual behaviour is important because the assessment of erogenous sensation can be used to understand the underlying mechanisms leading to decreased sensitivity/sexual arousal, sexual dysfunction, and related medical impairments caused by various clinical conditions including cancer, diseases affecting nerve functions, surgeries and ageing. (Krassioukov & Elliott, 2017; NITESCU, 2021) Brain areas such as the parietal operculum and posterior insula, mechano-afferents, particularly C-tactile (CT) fibres, and mechanosensitive ion channels like PIEZO2 have been implicated in responding to genital touch and sexual arousal, highlighting their role in the overall sexual experience. (Ackerley et al., 2014; George & Abraira, 2023; Lam et al., 2023; Walker et al., 2017)

Women have various erogenous zones that include more than just the genitals. Extra-genital areas like the breasts, nipples, lips, neck and inner thighs have been mentioned in several articles. These erogenous zones are frequently stimulated during intercourse and help women reach maximum pleasure. (Nummenmaa et al., 2016; Younis et al., 2016) Sexual breast stimulation, in particular, is not only an ancestral practice but also a crucial aspect of women's health. It plays an important role in promoting positive emotions, intimacy and overall well-being. (Robinson, 2015) With this said, it is fundamental to study everything evolving the mammary gland like its development,

histology, innervation and so on. Looking at how breast surgery impacts female's life and which techniques are available is also primordial because it can lead to impaired sensitivity and therefore, less pleasure. (Cieśla et al., 2020, 2021)

Finally, the aim of this work is to explore the complex mechanisms underlying erogenous sensation and sexual function, drawing on neuroscience research to deepen the understanding of human sexuality. Also, recognizing the breast as a crucial erogenous zone for women and emphasizing the importance of the mammary gland's anatomy, histology, vascularization and innervation in breast surgeries, in order to maintain full sensation.

## 2. EROGENOUS SENSATION

### a) Sex and the brain

Human erogenous sensitivity embraces an interplay between the peripheral and central nervous systems, its brain regions and specialized receptors, profoundly influencing sexual behaviour and intimate experiences. Through meticulous research and investigations, the connections between these elements have unveiled new dimensions in understanding human sexuality. (Calabrò et al., 2019)

The human sexual response cycle is a series of physiological changes activated by erotic stimuli. It involves vasodilation, genital swelling, increased blood pressure, and release of body fluids, ultimately preparing the body for sexual intercourse. As the human body undergoes various physiological changes at a rapid pace during sexual response, a more careful categorization of such changes using the scientific method was required. For this reason, Masters and Johnson proposed a four-stage model to explain these changes, which they believed to be the same in both men and women. So, the four consecutive stages of the human sexual response in order are: excitement, plateau, orgasm, and resolution. The excitement phase refers to the physiological manifestations of the body that enable sexual activity such as the vaginal lubrication and the swelling of the labia and clitoris. The plateau phase is when the intensity of excitement is at its maximum remaining static until orgasm is reached. The duration of this phase is uncertain and varies from person to person. In these two phases the body builds up

neuromuscular tension to be released during the orgasm. The orgasm phase is related to the sexual climax and after, in the resolution phase, the body reverts to normal conditions (non-excited state). (Masters & Johnson, 1966)

In 1974 Kaplan criticizes this model of Masters and Johnson dividing the human sexual response cycle in only three phases: desire, excitement and orgasm. The main difference in this triphasic model is that it includes psychological components like motivation and attention in the first phase. For Kaplan, the desire phase, encompasses a motivational component, meaning there is a motivation for engaging in sexual activity through sensory stimuli (i.e., vision, smell, touch, etc.), as well as through memories of erotic experiences and fantasies. (Kaplan, 1974)

Nowadays we use the theoretical approach used in the DSM manuals that is based on both of these models. It characterizes the sexual response cycle in four phases: desire, excitement, orgasm, and resolution, with the latter receiving much less attention. Sexual disorders in the DSM are based on the perspective that desire and excitement are part of the same phase in women but not in men. The desire phase is characterized by the willingness to engage in sexual activity, with or without sexual fantasies. Desire can be defined by self-initiative or by being receptive to another's initiative. Excitement is represented by physiological changes that enable sexual activity, visible in women through vaginal expansion and the engorgement of external vaginal organs. The orgasm phase is characterized by a rapid and abrupt increase in physiological activation, resulting in intense pleasure, a sensory climax that some may describe as "maximum sexual pleasure", and rhythmic contractions of the perineum muscle and reproductive organs. The final phase, the resolution, generally involves feelings of well-being and tranquillity, along with a variable decrease in sexual excitability. (Fauman, 2002)

Sexual desire, arousal and orgasm are mediated by complex, yet still not fully understood, interactions of the somatic and autonomic nervous systems. Somatic pathways convey tactile and proprioceptive signals from the genitalia and other erogenous zones to the brain, contributing significantly to sexual arousal. Conversely, the autonomic nervous system modulates physiological responses during sexual activity, orchestrating changes in heart rate, blood pressure and genital blood flow. The

disruption in these pathways can negatively impact people's sex function. (Calabrò et al., 2019)

But the best way to study the sexual pleasure cycle, in order to comprehend its neurologic involvement, is dividing it in wanting, liking and inhibition. In this way it's easier to compare it to other motivations (thirst, hunger, addiction) and across species. Wanting is driven by mesolimbic dopamine while liking is driven by opioid systems. (Georgiadis & Kringelbach, 2016)

In animal studies it was found that afferent sensory input from the genitalia triggers primal sexual reflexes, including spinal cord reflexes (erection, lubrication, ejaculation) (Normandin & Murphy, 2011) and behavioural responses (female receptive posture, male mounting behaviour) which may also be present, in a rudimentary form, in humans. The sensory information from the genitalia reaches centres in the brainstem and diencephalon that organize these reflexes, notably the midbrain periaqueductal grey matter (PAG) and the hypothalamus, linked to such behaviours in species like mice. (Hull & Dominguez, 2007; Pfaus, 2009; Sakuma & Pfaff, 1979) However, connections from the external genitalia extend to various brain regions. Studies in rats revealed the involvement of multiple brain areas, including the PAG and parabrachial nucleus (brainstem), amygdala, hypothalamus, and nucleus accumbens. (Marson, 1995; Marson & Murphy, 2006) Another approach involves identifying neural activity during actual sexual performance, typically involving genital stimulation. Here the intervention of the hypothalamus, amygdala, bed nucleus of the stria terminalis, and thalamus was discovered in both males and females. Unfortunately, there is limited information on cortical activity in animal models, despite the cortex being a probable target for genital sensory information. (Coolen et al., 1998; Veening & Coolen, 1998)

Research on the neural processing of genital touch in humans, draws from functional neuroimaging in healthy individuals and neurological patients. While animal studies focus on subcortical structures like the thalamus and hypothalamus, human studies primarily examine the cortical representation of the genitalia, particularly in the primary somatosensory cortex in the postcentral gyrus (S1). The iconic "homunculus" shows genitalia representation on the paracentral lobule, although its accuracy is debated due to discordances seen when applied genital stimulation. (Bradley et al., 1998; Georgiadis et al., 2010; Penfield & Rasmussen, 1950) Studies corroborate the general location of

genital representation in the postcentral gyrus, but the precise location remains controversial. (Guérit & Opsomer, 1991; Mäkelä et al., 2003) While S1 may contribute to genital sensations, it may not be sufficient for sexual feelings, which likely involves interactions with other brain areas. Areas like the parietal operculum and posterior insula respond to genital touch and sexual arousal, suggesting their involvement in the overall sexual experience. (Kell et al., 2005; Kortekaas et al., 2015; Mäkelä et al., 2003) However, the involvement of subcortical areas in human genital touch remains unclear, despite evidence given from animal studies. (Georgiadis & Kringelbach, 2016)

Touch is perceived through mechano-afferents in the peripheral nervous system that innervates the skin. These divide into two groups: myelinated, fast conducting A fibres and unmyelinated, slowly conducting C-tactile (CT) fibres. Focusing on CT fibres, only present in hairy skin, they respond optimally to slow stroking stimulation, light force and temperatures around 32ºC. These characteristics resemble interpersonal and pleasant touch (Ackerley et al., 2014; Löken et al., 2009; Olausson et al., 2010) and also because CTs trigger oxytocin release known for facilitating social behaviour. But these fibres were also found to influence the perception of erotic stimuli, creating an emotional platform that increases the likelihood of sexual feelings. (Lee et al., 2009; Walker et al., 2017)

The connection between gentle touch, CT fibres, and eroticism prompts inquiry into whether a similar relationship exists for genital skin. While the genital area is widely recognized for its heightened erotic sensitivity, it remains uncertain whether CT fibres are present here. Typically, CT fibres are associated with hairy skin due to their association with hair follicles. (Abraira & Ginty, 2013) However, the glabrous skin of the glans penis and glans clitoris, devoid of hair, harbours a dense concentration of unmyelinated fibres. The exact role of these fibres in sexual sensation is still under debate. (Halata & Munger, 1986; Shih et al., 2013)

### b) Erogenous zones

Sexual arousal can be triggered by touching practically all areas of the body, with specific hotspots which we call erogenous zones. These may be genital or extragenital and are parts of the body that when touched are sexually arousing and, a lot of these extra-genital zones, when stimulated, can induce orgasm. In one study, 95.3% of female

participants said “yes” when asked about feeling erogenous sensations once touched in body parts besides the genitalia, and 12% of them reported reaching orgasm following their stimulation. Important to note that, of these 12%, all of them reported as the source of their orgasm being the breasts/nipples and added that the orgasm was equivalent or stronger than the ones provoked by stimulating the genitals. (Younis et al., 2016) Even if it isn’t in a direct way, stimulating extra-genital parts during foreplay helps women reach climax and a short amount of foreplay is a big complain between the female community. (Nagao et al., 2014) The breasts, nipples, lips, neck, ears, buttocks and inner thighs are considered powerful erogenous zones and women have a greater diversity of these areas compared to men.

Touching is a strong way to elicit sexual arousal whether is being touched by someone or touching ourselves. (Nummenmaa et al., 2016; Younis et al., 2016) But sexual interactions don’t just involve being touched, it includes as well touching others and mutually looking at each other’s bodies. Sexual arousal isn’t a unisensory experience although touch is a primary character in the majority of sexual interactions. Visual stimulation, in the form of being looked at and appreciating the partner’s physic characteristics is also arousing. (Kühn & Gallinat, 2011; Redouté et al., 2000) This suggests that stimulating erogenous areas plays a crucial role in interpersonal relations serving, for example, as a pair-bonding function, via stimulation of CT fibres. (Dunbar, 2010; Morrison et al., 2011)

Research on the mechanosensitive ion channel PIEZO2 sheds light on its significance in perineal mechanosensation and sexual function. Activation of PIEZO2 receptors in nerve endings surrounding hair follicles leads to the transmission of electrical signals through low-threshold mechanoreceptors, like the CTs presented before, to the spinal cord, inducing pleasurable sensations when reaching the brain. (George & Abraira, 2023) Studies have shown that individuals with biallelic loss of PIEZO2 function exhibit severe hyposensitivity in genital sensation, impacting their ability to experience direct pleasure from gentle touch or vibration. It is also demonstrated that PIEZO2 function is key for triggering touch-evoked erection reflexes and successful mating in mice. The absence of PIEZO2 leads to a profound loss of behavioural responses to gentle peri genital touch, showing its importance in mediating physiological responses needed for sexual function.

The findings suggest that this ion channel is essential for detecting subtle stimuli in the genital region and initiating important sexual responses. (Lam et al., 2023)

Analysing the sensibility of the body in regard to light touch, pressure and vibration is important to comprehend the best way to elicit sexual arousal in each body part. The genitals can be considered as primary sexual zone, breasts and neck as secondary sexual zone and forearm and abdomen as neutral zones. Regarding pressure, studies show that the clitoris and nipple appear to be the most sensitive parts with not much difference between these primary and secondary sexual zones. In terms of vibration, the clitoris beats all the other parts which is consistent with the use of many sex toys. But within the breasts, the highest sensitivity is found in the nipple followed by the areola. Light touch at last, presents significant differences between the three zones. In this case, the neutral zone is the most sensitive which is an interesting finding. (Cordeau et al., 2014)

### c) Sexual dysfunction

Sexual dysfunction poses challenges to people in a lot of ways and can have a major impact on their quality of life.

The DSM-IV divides sexual dysfunction in relation to the phases of the human sexual response cycle. Concerning sexual desire disorders, we have two categories: Hypoactive sexual desire and sexual aversion. Hypoactive sexual desire is defined as persistent or recurrent absence of sexual fantasies and desire for sexual activity, and in a 1994 study, 33.4% of women reported a lack of sexual interest for a several amount of time. Sexual aversion relates to persistent or recurrent avoidance of sexual genital stimulation with a partner.

Moving on to sexual arousal disorders, regarding women, we have the female sexual arousal disorder (FSAD) which refers to the inability to attain or maintain until the end of the sexual activity an "adequate lubrication-swelling response of sexual excitement". (Fauman, 2002; Laumann et al., 1994) Tactile sensitivity, by itself, may be associated with FSAD because of individuals' differences in noticing tactile sensations. This condition can be caused by lower levels of tactile receptors (KRANTZ, 1958) or by a different process of the nervous system regarding these receptors' signals. Normally, the problem is the amount of stimulation needed for the brain to percept it. (Johansson

& Vallbo, 1979) Abnormalities in the vascular mechanism can affect sexual arousal, such as low vaginal lubrification because genital tissue is dependent on an adequate blood flow. The mechanism behind this relation is the increasing of tactile threshold when the genital tissue becomes engorged with blood. (Rowland, 1998; Rowland et al., 1993) The threshold is much higher in women suffering from FSAD thereby conditioning their difficulty in feeling erogenous sensations. Causes of decreased blood flow to the genitals that can be easily changed in peoples' routine are smoking, consumption of alcohol and hypertension. (Depalma et al., 1987; Okabe et al., 1999) Anxiety and cognitive distraction have also been associated with sexual dysfunction. Studies have noted that this agitated mental state in women suffering from FSAD makes them less likely to note physical sensations during intercourse. (Beck et al., 1987; Geer & Fuhr, 1976) A study conducted by Frohlich and Meston discovered that diminished sensitivity in the index finger, which is not a primary erogenous zone, is associated with FSAD. This is a very interesting point because it suggests that the underlying mechanism of sexual dysfunction may be a physiological process which also means that it is systemic. It shows that a vascular dysfunction or a psychological process (like anxiety or distraction) affects measurement of tactile stimuli in the entire body. As a conclusion of the investigation, they demonstrated that the finger could serve as a marker for sexual arousal disorder. (Frohlich & Meston, 2005)

Biological involution, a natural consequence of aging, also significantly impacts sexual function, resulting in decreased arousal and libido. The decline in excitability threshold of erogenous zone receptors, plays a crucial role in this decline, impairing the perception of sexual stimuli. These irreparable biological phenomena explain and justify the difficult treatment of sexual dysfunctions in the elderly. Another group of factors that can contribute to this impairment are physiological, phycological, social and emotional factors. The state of sexual arousal is determined by neuro-psychic factors sensitized by visual, auditory, olfactory and tactile stimuli. (NITESCU, 2021) In the context of disabilities, the sexual arousal should slowly return to normal when the patient adapts to his condition, except when the cause of this "illness" is iatrogenic or continuing factors like pain or depression. In these cases, it continues to negatively affect sexual drive.

Since innervation travels through the spinal cord, addressing pathologies like spinal cord injury (SCI) is important due to lack of sensation in erogenous zones like the genitalia. Studies concerning sexual dysfunction following SCI have been conducted in order to better comprehend this pathology and learn how to approach it in the best way possible. SCI patients' sexual health is not only affected by the injury but also by the social, cultural and even personal stigma to view all sexual activities as pleasurable. (Krassioukov & Elliott, 2017) These investigations have shown that orgasm is only attainable in 50% of women with SCI and that besides this, they also suffer from intimacy problems that affect their day-to-day. (Sipski et al., 1995) Patients with this condition should go through a sexual rediscovery to find new ways, like appreciate the remaining sensations of their body to the fullest, to restore their quality of sexual life.

Promoting mindfulness and awareness to ones' sexual signs, even those that come from non-genital sources (ears, nipples, neck, hair), is a crucial tool in sexual dysfunction. (Brotto et al., 2016)

## 3. THE BREAST

### a) "Breast love"

Sexual breast stimulation is not only an ancestral practice but also a crucial aspect of women's health. It plays an important role in promoting positive emotions, intimacy and overall well-being. (Robinson, 2015)

Oxytocin is a neurotransmitter and hormone, also known as the bonding or love hormone, released from the pituitary gland of the brain. It is a powerful uterotonic agent that causes contractions of the uterus during birth (Fuchs et al., 1982) and is used to prevent postpartum haemorrhages. (Maughan et al., 2006) In women, this hormone is liberated during breastfeeding, but also with sexual arousal and orgasm, both associated with breast sex. (Carmichael et al., 1987; McNeilly et al., 1983) Also, animal studies have shown that oxytocin is crucial for pair bonding and reduction of stress. (Neumann, 2008) Therefore, it is understandable its reference as love hormone. It's related to nipple excitation, lovemaking, orgasm, uterine contractions, milk ejection, reduction of stress and it promotes pair-bonding. (Robinson, 2015)

The maximum pleasure of sex, for females, occurs when the uterus contracts during orgasm and it has been found that breast stimulation alone can induce this. The physiological connection between breast eroticism and uterine eroticism suggests that women's recognition of the profound pleasure derived from this association likely preceding the widespread acceptance and practice of sexual breast love. (Masters & Johnson, 1966)

In the topic of health, breastfeeding has been shown to offer protective benefits against various gynaecological cancers, including in-situ cervical cancer (Brock et al., 1989), endometrial cancer of the uterus (Newcomb & Trentham-Dietz, 2000), ovarian cancer (Grimes & Economy, 1995) and breast cancer. This protective effect highlights the multifunctional role of the breast, including sexual breast stimulation, which some women use to enhance sexual arousal and achieve orgasm. It suggests that this practice may also contribute to reducing the risk of these cancers (Murrell, 1991), as well as providing protection against sexual dysfunction and mental depression. (Robinson, 2015)

### b) Development of the mammary gland

Embryonic breast development, both in males and females, involves sequential interactions between a multitude of specialized cells. (Cieśla et al., 2020)

Breast tissue originates from specialized glands called mammary glands, which are a type of highly specialized apocrine glands. Their formation commences during the 4th week of gestation when the ectodermal cells undergo a double thickening in the ventral part of the embryo, forming the mammary line. This line extends from the axilla to the groin area on both sides. Although most of these structures regress during human foetal development, the rudiments of mammary glands persist on each side at the 4th intercostal space along the anterior chest wall. By 5th week, the remaining ectodermal tissue proliferates deeper into the skin, giving rise to the initial formation of breast buds. (PANDYA & MOORE, 2011) The foetal development progresses and by week 10, the original breast bud undergoes division, forming branches that by week 12 evolve into secondary breast buds that, ultimately, form the lobules found in mature breasts. Growth factors and hormones from both the extracellular matrix of the mesoderm and

adipose tissue, drive the primordial breast bud's development. In the subsequent phase, from week 12 to 20, the secondary buds of glandular tissue extend and branch into narrow channels, which will eventually mature into lactiferous ducts. This process is instigated by placental hormones, such as progesterone, growth hormone, insulin-like growth factor, oestrogen, prolactin, corticoids and triiodothyronine. The outcome of this hormonal cascade is the formation of glandular lobules containing their own exosecreting lactiferous ducts. (Hall, 2016; Macéa & Fregnani, 2006; Stone & Wheeler, 2015)

The developing breasts receive support through the process of skin raising and the formation of Cooper's suspensory ligaments, which secure the breasts within the fascia of the pectoralis major muscle. Lactiferous ducts, responsible for milk secretion, converge into the retro-areolar region, creating a recess and an opening in the skin, prompting the formation of a noticeable protrusion on the skin known as a breast nipple bud. This bud contains numerous longitudinally and circularly arranged smooth muscle fibres.

During the 5th month of foetal development, the areola surrounding the nipple and its apocrine Montgomery glands begin to form from the ectodermal tissue. Pigmentation of the nipple initiates around the 32nd week of gestation and continues until the end of pregnancy. (Hassiotou & Geddes, 2013; Lemaine & Simmons, 2013; PANDYA & MOORE, 2011)

Shortly after birth, proliferation of surrounding tissues leads to permanent raising of the nipple and slight pigmentation of the areola. In males, strong stimulation from testosterone via mesoderm receptors leads to rapid involution of glandular tissue, inhibiting breast development during the neonatal period. Contrarily, in females, oestrogen promotes further breast development and maturation. (Hall, 2016; Stone & Wheeler, 2015)

Throughout puberty, there is significant growth of the breasts. Initially, this involves the accumulation of adipose tissue and connective tissue around the ducts, followed by the expansion of glandular tissue and elongation of breast ducts. These changes are driven by oestrogen, growth hormone, prolactin and without the involvement of progesterone. Typically, breast development in women is achieved around the age of 20. (PANDYA & MOORE, 2011; Stone & Wheeler, 2015)

The breasts suffer no other processes until the woman gets pregnant. During pregnancy, they undergo significant changes, hormone influenced, to prepare for lactation. Following delivery, environmental factors (like neonate's crying and sucking) and intensive hormonal changes (such as prolactin, somatomammotropin and oxytocin) stimulate lactocytes in the follicles to produce milk, which is released from the nipple. (Ramsay et al., 2004, 2005) As breastfeeding ends, milk production diminishes due to reduced mechanical stimulation of the breasts and declining prolactin levels, causing the follicles to return to a resting state.

After 40 years of age, normally when women reach menopause, the decrease of hormonal stimulation occurs and contributes to the disappearance of the glandular tissue, which is replaced by connective and adipose tissue, leading to the permanent rest of the breasts. (Cieśla et al., 2020)

### c) Histology of the mammary gland

The glandular tissue of the breast, known as the mammary gland, contains several alveoli that together form lobules. These lobules joined form structures called lobes, which are surrounded by connective tissue. Alveoli have two layers: the internal, made of lactocytes responsible for the secretion of milk during lactation, and the external made of muscle-epithelial cells. Similarly, lactiferous ducts start in lactiferous follicles that form interlobular ducts and these ones form interlobar ducts. The main ducts begin at a distance of 8mm from the areola surface and their walls are made of flexible connective tissue containing elastic fibres and smooth muscle cells. The subcutaneous tissue of the areola is also composed by a big quantity of smooth muscle fibres. (Cieśla et al., 2020) Recently, authors have reported that there are 9 lobes and ducts on average discharging to the nipple of each breast. (Love & Barsky, 2004)

The breast's histology is a complex arrangement that contributes to its function and structure. There are two main components: the epithelium and the stroma. The duct-lobule organisation is made of two layers of epithelial cells (luminal and myoepithelial) surrounded with stroma and on top of the basal lamina. This lamina is what separates the ducts from the stromal tissue and is composed by collagen and laminin. (Hall, 2016; Lemaine & Simmons, 2013) Then, there are two types of stromal tissue: the intralobular

and the interlobular. The first one contains fibroblasts, lymphocytes, macrophages, plasmatic cells, blood vessels, it is rich in mucus and responds to hormone stimulation. The second one contains more collagen fibres because it forms the connective tissue around the lactiferous ducts. It's this part of the mammary gland that is replaced by adipose tissue during menopause and influences the most breast size. (Gastounioti et al., 2018; Saeed & Shousha, 2014)

In the skin of the NAC (nipple-areola complex), we can find melanocytes, responsible for the pigment of this area, sebaceous glands known as Montgomery's tubercles and apocrine glands. This skin lies on a layer of smooth muscle which, below the areola, has adipose tissue that disappears towards the nipple. In the peri-areolar area the skin is directly attached to the glandular tissue by suspensory ligaments, subcutaneous muscles and nipple muscle. This complex also includes a developed network of blood vessels, lymphatic vessels, sensory nerve endings and smooth muscles containing the sympathetic system fibres.

Study of the fascia is crucial for breast surgery. This tissue is highly innervated and vascularised besides surrounds muscles and organs. Nerve endings, in the form of mechanoreceptors, are located in the deep fascia giving it an important role on deep sensibility (proprioceptive). Furthermore, the fascia is a source of multipotent stem cells responsible for the process of tissue repair. (Cieśla et al., 2020) The skin of the breast and the superficial fascia are connected by the ligaments of Cooper known for its role in fixating the mammary gland to the skin. (Lockwood, 1991; A. Stecco et al., 2009)

The most essential fascial component is the inframammary fold located in the lower edge of the greater pectoral muscle. This structure is made of the superficial part of fascia, which extends transversely at the level of the 5th rib thanks to the ligaments of Cooper. Apart from the already mentioned function of suspending the mammary gland on the chest wall and shaping the breast, the ligaments create a path for vessels and nerves to enter directly from the chest wall to the mammary gland and make its way to the NAC. Also, its system of numerous subcutaneous connections, between the superficial and deep fascia, needs to be preserved for immediate breast reconstruction. Because of the need to create a pocket under the pectoral muscle, any damage to the inframammary fold makes it impossible to perform immediate reconstruction. (Cieśla et al., 2020; Nava et al., 1998; Riggio et al., 2000; C. Stecco & Stecco, 2012)

**d) Vascularization and innervation**

The vascularization of the breasts displays considerable individual variation. However, certain consistent elements include the internal thoracic artery along with the lateral thoracic artery, the thoracoacromial artery, terminal branches of the perforators from the 3rd to 8th intercostal arteries, and small vessels that supply blood to the serratus anterior muscle. (Ho et al., 2016; Van Deventer & Graewe, 2016)

Regarding the venous outflow from the mammary gland, the main pathway is the axillary vein, that transforms into the subclavian vein when it passes the clavicle. A significant anatomical component is the subareolar venous plexus from where the blow outflows and takes one of the two possible paths: superficial or deep. The superficial starts under the areola and drains to the internal thoracic vein and superficial veins of the lower part of the neck. The deep, under the superficial fascia, drains also to the internal thoracic vein or to the posterior intercostal veins or directly to the axillary vein. (Losken et al., 2014; Würinger et al., 1998)

The lymphatic drainage of the breast involves a complex network of vessels and nodes. Lymph from the mammary gland starts in the intercellular spaces of glandular tissue lobules and flows through non-valvular lymph capillaries into pre-collectors with valves, located in the dermis. These connect to deep lymph collecting vessels under the deep fascia, forming the Sappey plexus under the areola. (Sappey, 1874) Breast lymph vessels form four interconnected plexuses: cutaneous (skin), subcutaneous, fascial (greater pectoral muscle), and glandular (lobules, lobes, lactiferous ducts). (Ahmed et al., 2016; Borm et al., 2019) Lymph from the subareolar plexus drains primarily to axillary lymph nodes and internal thoracic nodes. Additionally, interconnections between both breasts can cause cross-metastases. Axillary lymph nodes, the primary filters, are categorised into five groups: lateral thoracic, acromial, subscapular, central axillary, and subclavian nodes. Most breast lymph (80-90%) drains through the first level of axillary nodes. Other routes include pathways along the internal thoracic artery and direct drainage to nodes behind the ribs or to the liver (Gerota's pathway). (Barros et al., 2016; Würinger et al., 1998) Understanding the circulation of interstitial fluid within the breast provides valuable insight into the importance of precise surgical incisions and proper soft tissue manipulation during oncoplasty. By comprehending the pathways of lymph drainage from the mammary gland, surgeons can enhance their planning and execution

of surgeries for patients with breast cancer. This understanding enables more effective strategies to preserve lymphatic pathways and minimize postoperative complications. (Cieśla et al., 2021)

Moving on into the innervation of the mammary gland it is supplied by nerves from both the somatic peripheral nervous system and the autonomic sympathetic system. Notably, there are no parasympathetic nerve endings within the breast tissue. The innervation of the breast, as well as the skin covering the anterior-lateral area of the chest, is closely interconnected. This correlation is shown by the shared ectodermal origin of both structures. (Lemaine & Simmons, 2013) Exploring, in particular, the sensory innervation of the nipple is essential because it plays an important part in both physiological functions, such as breastfeeding and sexual arousal. To secure its functions, the nipple is supplied by somatosensory nerves that convey pressure, light touch, temperature and nociceptive stimulus to the central nervous system. (Gutiérrez-Villanueva et al., 2020) The innervation of the breast skin and anterolateral chest wall comes from anterior and lateral cutaneous branches of the intercostal nerves second through sixth. Also, the skin of the upper portion of the breast is innervated by anterior branches of the supraclavicular nerve arising from the cervical plexus. The NAC is supplied by the anterior and lateral cutaneous branches of the intercostal nerves third through fifth and the branches of the fourth intercostal nerve where found to supply the largest surface area of the breast skin and NAC. (Bland et al., 2017; PANDYA & MOORE, 2011; Smeele et al., 2022) Because of this consistency, of the anterior and lateral cutaneous branches of the fourth intercostal nerve being responsible for a great amount of the breast innervation, these nerves are very important in reconstructive and cosmetic breast surgery in order to avoid postoperative numbness of the nipples. (R. J. Levin, 2006)

All the studies related to the breast innervation highlight the variability in nerve innervation patterns of the female breast, underlining the weight of individualized approaches.

### e) The nipple-areola complex (NAC)

The NAC comprehends the nipple, areola and surrounding tissues. Evolutionarily, the development of this complex is intricately linked to lactation and maternal-infant bonding, however, in human sexuality, the NAC transcends its primary role in lactation to become a site of sexual attraction and pleasure and is the most erogenous site of the breast. (R. J. Levin, 2006) A study conducted by Benedetto Longo and his team, proved that the nipple is more sensitive than the areola and that NAC from smaller breasts are statistically more sensitive than the ones from macromastia women. (Longo et al., 2014)

The nipple can become erected by various tactile stimulations, such as cold, sexual touch, breast-feeding and so on. This can induce the milk ejection reflex or sexual arousal because of its intense sensory innervation. This phenomenon of erection occurs via activation of the sympathetic nervous system and the contraction of the nipple's internal smooth muscle. (Tezer et al., 2012) But it's less known that the areola also becomes prominent during sexual arousal. This simultaneous erection of the nipple and areola represents the initial response of the breast to sexual stimulation. Additionally, during the late excitement phase, often referred to as the Plateau phase, the inner surfaces of the breasts may exhibit a mottled, red flush known as the "sex flush." This erythematous maculo-papular rash typically originates from the epigastrium and can spread to cover the entire breast. It's worth noting that this flush is discharged upon reaching orgasm. (Cathcart et al., 1949; R. J. Levin, 2006)

Circling back to nipple erection (NE), there's a study about the existence of nitric oxide synthase (NOS) in the NAC in order to explain this mechanism of sexuality. Nitric oxide (NO) is a low weight and short half-life molecule that can easily diffuse across membranes independent of receptors. It has a lot of different effects according to the organ involved but it's known for its blood-flow regulation, smooth muscle relaxation and muscle contractility control. The study was able to find that NOS is in fact present in the NAC and probably involved in NE by mediating the relaxation of vascular and nonvascular smooth muscle. (Tezer et al., 2012)

Levin and Meston conducted an investigation about the effects of nipple and breast stimulation on sexual arousal, offering understandings into gender-specific responses to such stimuli. Their findings unveil distinct patterns in how men and women react to nipple and breast stimulation. Among the participants, women displayed a remarkable

sensitivity to nipple stimulation, with a significant proportion reporting heightened sexual arousal and desire. Specifically, 81.5% of women acknowledged that nipple and breast stimulation caused or enhanced their sexual arousal. Additionally, a considerable percentage, totalling 78.2%, agreed that such manipulation increased their arousal when they were already sexually stimulated. Furthermore, 59.1% of women admitted to requesting nipple stimulation during lovemaking, revelling the profound impact of nipple stimulation on their sexual experiences. Only a minor fraction of female, comprising 7.2%, reported a decrease in arousal following nipple stimulation. In contrast, men exhibited more varied responses to the stimulation. While a significant percentage, amounting to 51.7%, acknowledged that nipple stimulation caused or enhanced their sexual arousal, it was notably lower compared to women. Moreover, only 39% of men agreed that such manipulation increased their arousal when already sexually stimulated and a mere 17.1% reported requesting nipple stimulation during sexual activities. Similarly, a small fraction, comprising 7.5%, found that nipple stimulation decreased their arousal. These findings underline the gender-specific nature of responses to nipple and breast stimulation, highlighting the pronounced sensitivity of women to such stimuli compared to men. (R. Levin & Meston, 2006)

To finish this topic, a study conducted by Krychman and others, aimed to investigate the effects of a novel topical formulation, RJ101, applied to the NAC on female orgasm. The researchers found that stimulating the adrenergic nerves in the smooth muscle of the NAC using RJ101 led to increased nipple erection, sensitivity and positive benefits for sexual function. By inducing nipple erection, the NAC sensitivity increased by 20%, resulting in improvements in orgasmic intensity, pleasure and overall satisfaction. Overall, this study highlights the potential benefits of adrenergic nerve stimulation in improving sexual function. The results support the notion that enhancing NAC sensitivity through topical application can positively impact female sexual response, particularly in the domain of orgasm. (Krychman et al., 2020)

## 4. BREAST SURGERY IMPACT ON SENSITIVITY

### a) Sensitivity preservation

Preservation of sensitivity is one of the most important goals in breast surgery. Anatomical studies based on various dissections regarding the innervation of the nipple-areola region, mentioned the 4th intercostal nerve, making it a very important one for this complex. (Hefter et al., 2003)

Clinical studies are important for a better understanding of breast innervation, particularly involving breast reduction and breast reconstruction surgeries:

### b) Breast reduction

According to the American Society for Aesthetic Plastic Surgery, in 2017, breast reduction was the seventh most performed surgery. In fact, patients often undergo this kind of procedure not only for aesthetic aspects but also for functional reasons. For example, breast hypertrophy causes skin lesions to the inframammary fold area, back pain due to the weight and loss of self-confidence. (Schlenz et al., 2005; The American Society for Aesthetic Plastic Surgery, 2017)

In breast reduction surgeries, the preservation of the breasts' sensitivity is an important achievement. Several reports have attributed this lack of sensation to the weight of resection rather than the surgical technique used. (Gonzalez et al., 1993; Slezak, 1993) But more recent studies say otherwise. (Greuse et al., 2001; Hamdi et al., 2001) Delvecchyo, with an innovative dermal somatosensory method, assessed the sensibility of five regions of the breasts (the four quadrants and the nipple) of two groups. Group 1 were small breasted and unoperated women, while Group 2 were macromastia patients presenting for breast reduction surgery. The small breasts were more sensitive than the preoperative large ones but, after the reduction surgery, there was a significant improvement in sensibility making the sensibility of both groups similar. (DelVecchyo et al., 2004) In agreeance, Schlenz in his study with 74 women comparing five surgical techniques and the weight of resection, also found that changes in breasts' sensitivity were not related to the amount resected but to the technique used. (Schlenz et al., 2005)

The optimal pedicle approach in mammaplasty has changed over time and there are various studies defending the different techniques. Despite the fact that in the literature no reduction technique has proven to be the best, the most commonly used is the inferior pedicle (IP) reduction although the superomedial pedicle (SMP) technique has gaining more acceptance lately. The IP is considered to provide the best vascularization while at the same time allowing safe removal of large amount of tissue. (Okoro et al., 2008) The arising of SMP is due to its supposedly better cosmetic outcome with less "bottoming out" and shorter operative time without increased risk of NAC's necrosis. (Brownlee et al., 2017) However, no real evidence exists to support mostly one of the two techniques presented.

Besides the pedicle approach used during surgery there are two different scaring. The wise pattern reduction, also known as inverted-T, that implicates three incisions: peri-areolar, vertical extending downward from the areola to the inframammary fold (IMF) and horizontal along the IMF. And the vertical reduction which only requires two incisions: peri-areolar and vertical. (Ogunleye et al., 2017)

A recent investigation to compare the IP and SMP techniques was conducted using in both of them the wise pattern breast reduction. After two years follow-up of 58 patients the conclusion was that the SMP approach provides stable and satisfactory results for women in terms of shape, size and appearance. Also, discovered that SMP improves some of the biggest concerns regarding the use of IP like lower pole elongation and ptosis recurrence. (Sapino et al., 2021)

Regarding erogenous sensation, all breast reduction surgeries aim to maintain it and surgeons often discuss the pros and cons of each technique with patients to determine the most suitable approach based on their specific needs and goals. Breast reduction is actually associated, in general, with sexual quality of life, sexual well-being and lower incidence rate of sexual dysfunction in patients suffering from macromastia. (Janik et al., 2019)

### c) Breast reconstruction

Breast cancer is a global cause for concern owing to its high incidence around the world. It has now overtaken lung cancer as the world's mostly commonly diagnosed

cancer, according to statistics released by the International Agency for Research on Cancer in December 2020. In 2022 it was the most common cancer in women in 157 countries out of 185. (World Health Organization, 2021, 2024)

Women who undergo a mastectomy, a surgery to remove an entire breast to treat or prevent breast cancer, have the option to reconstruct the removed breast. Breasts can be rebuilt using implants (either saline or silicone) or autologous tissue, also known as flap, a piece of tissue containing skin, fat, blood vessels, and sometimes muscle taken from elsewhere in a woman's body. Sometimes a combination of implants and autologous tissue is used. Flaps used for reconstruction most often come from the abdomen or back, however, they can also be taken from the thighs or buttocks. Depending on their source, flaps can be considered pedicled or free. With pedicled flaps the tissue and blood vessels are moved together to the breast and don't need to be reconnected, while with free flaps the tissue is cut free from blood supply, which means it needs to be attached to new vessels in the breast. An example of free flap is the DIEP (Deep Inferior Epigastric artery Perforator) flap that contains only skin, blood vessels, and fat, without the underlying muscle. (National Cancer Institute, 2017) One drawback of using free flaps is the reduced sensation in the reconstructed breast. During the harvesting of the tissue graft, all nerves within the tissue are not preserved. Traditionally, only vascular anastomosis is performed between the chest area and the flap, allowing for subsequent reinnervation of the breast to occur spontaneously from surrounding tissues. (Helena Puonti, 2017) TRAM (transverse rectus abdominis myocutaneous) flaps also come from the abdomen, but these ones include muscle and can be pedicled or free.

Breast reconstruction surgery can be performed at the same time as the mastectomy (immediate reconstruction) or after the mastectomy incisions have healed and cancer treatment is completed (delayed reconstruction). In the final stage of reconstruction, a nipple and areola may be created on the reconstructed breast if they were not preserved during the surgery. Occasionally, reconstruction also includes surgery on the contralateral breast to ensure both breasts match in size and shape. (National Cancer Institute, 2017)

Besides wanting symmetrical and shaped breasts, women also report the importance of having sensation. The loss of sensation in the reconstructed breast is both unpleasant

and unexpected, as noted in a 2017 New York Times article written by Rabin. (Rabin, 2017) Sensory nerve coaptation has been suggested as a potential solution to enhance postoperative sensation. The first innervated autologous breast reconstruction was performed in 1992 by Slezak et al., using the fourth lateral intercostal nerve and a mixed abdominal nerve in TRAM flaps. (Slezak et al., 1992) This technique was later refined to preserve motor branches. Allen and Treece were the first to apply this method to DIEP flaps. (Allen & Treece, 1994) More recently, Spiegel et al. introduced a new technique using the anterior branch of the third intercostal nerve as the recipient nerve. (Spiegel et al., 2013) Despite its potential benefits, the technique has not been widely adopted due to underestimation of its importance and a lack of scientific evidence. (Bubberman et al., 2023)

Microneurovascular transversal rectus abdominis muscle flap reconstruction of the breast:

The study of Helena Puonti focused on finding a way to dissect and reconnect nerves of the abdominal flap and the chest area, in order to provide breast cancer patients, undergoing reconstruction, with sensation. The study had three important aims: Finding which nerves in the chest and abdominal flap, when connected, would give the better sensation on the breast; Discover if the dissection of nerves with the abdominal flap would cause any extra complications in the donor; And develop a better neurorrhaphy procedure, with two pedicles, in order to provide better sensitivity to the breast.

This investigation comprehended 96 patients who underwent breast reconstruction with a free muscle-sparing transverse rectus abdominis myocutaneous flap (ms-TRAM flap), in which 44 of them the innervation was done with novel dual neurorrhaphy (technique using two nerve pedicles) and 32 with single neurorrhaphy (technique using one nerve pedicle). The rest of the patients, 20 in total, underwent reconstruction without neurorrhaphy to serve as the control group. At the end, she concluded that with the coaptation of any nerves available in the chest and abdominal flap, sensation of the ms-TRAM flap breast could be restored, regardless of the neurorrhaphy technique, although the innervation with two nerve pedicles resulted in better sensory recovery. The vibration and tactile detection recovered better than the thermal detection and

sharp-blunt discrimination but, it is known that after other breast cancer treatments, not including surgery, the tactile and thermal sensitivity are already affected and decreased. Puonti also discovered that, using single or dual neurorrhaphy didn't cause any new problems in the donor compared with the conventional non-innervated flap procedure. Patients were left with a minimal loss of sensation in a small area under the umbilicus. Besides, using these new techniques in surgery only increased the operative time in about 15-30 minutes, which isn't significant. Lastly, using the dual neurorrhaphy resulted in better outcomes regarding sensitivity of the reconstructed breast than the single neurorrhaphy. (Helena Puonti, 2017)

Based on the study of Helena Puonti we can infer that the innervation of free ms-TRAM flap, especially when associated with the dual neurorrhaphy, improves the sensibility of the reconstructed breast compared with the technique of using a non-innervated flap which is nowadays the main surgery approach. A use of this technique should be implemented in clinical practice because plastic surgeons are now more concerned with providing the most complete aesthetic and functional breast reconstruction possible, which includes the restoration of its erogenous sensation.

## 5. CONCLUSION

In conclusion, the exploration of the neural mechanisms underlying sexual pleasure and erogenous sensation offers a captivating insight into the intricate workings of the human brain and nervous system in the context of intimate relationships and sexual experiences. The research presented in this document not only sheds light on the complex interplay between sensory pathways, brain regions, and specialized receptors but also emphasizes the significance of understanding the physiological basis of sexual desire, arousal, and orgasm. Moreover, the identification of mechano-afferents, CT fibres, and the mechanosensitive ion channel PIEZO2 as key players in mediating erogenous sensation underscores the intricate processes that contribute to human sexual experiences.

In addition to the broader exploration of erogenous sensitivity, it is crucial to consider the specific role of the breasts as a significant erogenous zone in women's sexuality. Studies have highlighted the importance of breast stimulation in inducing sexual arousal

and pleasure, with research indicating that the breasts, nipples, and surrounding areas play a crucial role in sexual experiences and reaching maximum pleasure. Furthermore, surgical interventions involving the breasts, such as breast reconstruction following mastectomy, can have a profound impact on tactile sensitivity and sexual function. Understanding the neural pathways associated with breast sensitivity and the potential effects of surgical procedures on erogenous zones is essential for optimizing postoperative outcomes and enhancing the overall well-being of women undergoing breast surgeries. Studies examining the recovery of tactile sensitivity in patients undergoing breast surgeries, including procedures like lateral pedicle mammaplasty and microneurovascular transversal rectus abdominis muscle flap reconstruction, provide valuable insights into the complex relationship between surgical interventions and erogenous sensation. The research on nerve dissection and reconnection in breast cancer patients undergoing surgery to restore sensation in the reconstructed breast underscores the importance of preserving neural pathways. By integrating knowledge of neural pathways with surgical techniques aimed at preserving tactile sensitivity in erogenous zones, healthcare providers can optimize patient outcomes, such as a more complete functional breast reconstruction, and promote holistic well-being in individuals undergoing breast surgeries.

Overall, the intersection of neural mechanisms, erogenous sensitivity, and surgical impact on the breasts highlights the intricate nature of human sexuality and the importance of a multidisciplinary approach to understanding and addressing sexual health and well-being. By continuing to explore the neural circuits involved in sexual pleasure, erogenous sensation, and the impact of surgical interventions on tactile sensitivity, we can advance our knowledge of human sexuality and contribute to the development of comprehensive care strategies that prioritize the sexual health and satisfaction of individuals, especially women.

**REFERENCES:**

Abraira, V. E., & Ginty, D. D. (2013). The sensory neurons of touch. In *Neuron* (Vol. 79, Issue 4). https://doi.org/10.1016/j.neuron.2013.07.051

Ackerley, R., Backlund Wasling, H., Liljencrantz, J., Olausson, H., Johnson, R. D., & Wessberg, J. (2014). Human C-tactile afferents are tuned to the temperature of a skin-stroking caress. *Journal of Neuroscience*, *34*(8). https://doi.org/10.1523/JNEUROSCI.2847-13.2014

Ahmed, M., Baker, R., & Rubio, I. T. (2016). Meta-analysis of aberrant lymphatic drainage in recurrent breast cancer. In *British Journal of Surgery* (Vol. 103, Issue 12). https://doi.org/10.1002/bjs.10289

Allen, R. J., & Treece, P. (1994). Deep inferior epigastric perforator flap for breast reconstruction. *Annals of Plastic Surgery*, *32*(1), 32–38. https://doi.org/10.1097/00000637-199401000-00007

Barros, A. C. S. D., Mori, L. J., Nishimura, D., & Jacomo, A. L. (2016). Surgical anatomy of the internal thoracic lymph nodes in fresh human cadavers: Basis for sentinel node biopsy. *World Journal of Surgical Oncology*, *14*(1). https://doi.org/10.1186/s12957-016-0897-2

Beck, J. G., Barlow, D. H., Sakheim, D. K., & Abrahamson, D. J. (1987). Shock Threat and Sexual Arousal: The Role of Selective Attention, Thought Content, and Affective States. *Psychophysiology*, *24*(2). https://doi.org/10.1111/j.1469-8986.1987.tb00273.x

Bland, K. I., Copeland, E. M., Klimberg, V. S., & Gradishar, W. J. (2017). The Breast: Comprehensive Management of Benign and Malignant Diseases. In *The Breast: Comprehensive Management of Benign and Malignant Diseases*. https://doi.org/10.1016/C2014-0-01946-6

Borm, K. J., Voppichler, J., Düsberg, M., Oechsner, M., Vag, T., Weber, W., Combs, S. E., & Duma, M. N. (2019). FDG/PET-CT–Based Lymph Node Atlas in Breast Cancer Patients. *International Journal of Radiation Oncology Biology Physics*, *103*(3). https://doi.org/10.1016/j.ijrobp.2018.07.2025

Bradley, W. E., Farrell, D. F., & Ojemann, G. A. (1998). Human cerebrocortical potentials evoked by stimulation of the dorsal nerve of the penis. *Somatosensory and Motor Research*, *15*(2). https://doi.org/10.1080/08990229870844

Brock, K. E., Berry, G., Brinton, L. A., Kerr, C., MacLennan, R., Mock, P. A., & Shearman, R. P. (1989). Sexual, reproductive and contraceptive risk factors for carcinoma-in-situ of the uterine cervix in Sydney. *Medical Journal of Australia*, *150*(3). https://doi.org/10.5694/j.1326-5377.1989.tb136389.x

Brotto, L. A., Chivers, M. L., Millman, R. D., & Albert, A. (2016). Mindfulness-Based Sex Therapy Improves Genital-Subjective Arousal Concordance in Women With Sexual Desire/Arousal Difficulties. *Archives of Sexual Behavior*, *45*(8). https://doi.org/10.1007/s10508-015-0689-8

Brownlee, P., Chesire, D., Crandall, M., & Murray, J. (2017). Superomedial pedicle reduction mammaplasty: increased resection weight does not increase nipple necrosis. *Journal of Surgical Research*, *219*. https://doi.org/10.1016/j.jss.2017.05.114

Bubberman, J. M., Van Rooij, J. A. F., Van der Hulst, R. R. W. J., & Tuinder, S. M. H. (2023). Sensory recovery and the role of innervated flaps in autologous breast

reconstruction—a narrative review. In *Gland Surgery* (Vol. 12, Issue 8). https://doi.org/10.21037/GS-23-40

Calabrò, R. S., Cacciola, A., Bruschetta, D., Milardi, D., Quattrini, F., Sciarrone, F., la Rosa, G., Bramanti, P., & Anastasi, G. (2019). Neuroanatomy and function of human sexual behavior: A neglected or unknown issue? In *Brain and Behavior* (Vol. 9, Issue 12). https://doi.org/10.1002/brb3.1389

Carmichael, M. S., Humbert, R., Dixen, J., Palmisano, G., Greenleaf, W., & Davidson, J. M. (1987). Plasma oxytocin increases in the human sexual response. *Journal of Clinical Endocrinology and Metabolism*, *64*(1). https://doi.org/10.1210/jcem-64-1-27

Cathcart, E. P., Gairns, F. W., & Garven, H. S. D. (1949). XXIV.—The Innervation of the Human Quiescent Nipple, with Notes on Pigmentation, Erection, and Hyperneury. *Transactions of the Royal Society of Edinburgh*, *61*(3), 699–717. https://doi.org/10.1017/S0080456800019104

Cieśla, S., Wichtowski, M., Poźniak-Balicka, R., & Murawa, D. (2020). The surgical anatomy of the mammary gland (part 1.) General structure, embryogenesis, histology, the nipple-areolar complex, the fascia of the glandular tissue and the chest wall. *Nowotwory*, *70*(5), 211–219. https://doi.org/10.5603/NJO.2020.0042

Cieśla, S., Wichtowski, M., Poźniak-Balicka, R., & Murawa, D. (2021). The surgical anatomy of the mammary gland. Vascularisation, innervation, lymphatic drainage, the structure of the axillary fossa (part 2.). *Nowotwory*, *71*(1). https://doi.org/10.5603/NJO.2021.0011

Coolen, L. M., Peters, H. J. P. W., & Veening, J. G. (1998). Anatomical interrelationships of the medial preoptic area and other brain regions activated following male sexual behavior: A combined Fos and tract-tracing study. *Journal of Comparative Neurology*, *397*(3). https://doi.org/10.1002/(SICI)1096-9861(19980803)397:3<421::AID-CNE8>3.0.CO;2-4

Cordeau, D., Bélanger, M., Beaulieu-Prévost, D., & Courtois, F. (2014). The Assessment of sensory detection thresholds on the perineum and breast compared with control body sites. *Journal of Sexual Medicine*, *11*(7). https://doi.org/10.1111/jsm.12547

DelVecchyo, C., Caloca, J., Caloca, J., & Gómez-Jauregui, J. (2004). Evaluation of breast sensibility using dermatomal somatosensory evoked potentials. *Plastic and Reconstructive Surgery*, *113*(7). https://doi.org/10.1097/01.PRS.0000122210.12819.B8

Depalma, R. G., Emsellem, H. A., Edwards, C. M., Druy, E. M., Shultz, S. W., Miller, H. C., & Bergsrud, D. (1987). A screening sequence for vasculogenic impotence. *Journal of Vascular Surgery*, *5*(2). https://doi.org/10.1016/0741-5214(87)90131-5

Dunbar, R. I. M. (2010). The social role of touch in humans and primates: Behavioural function and neurobiological mechanisms. In *Neuroscience and Biobehavioral Reviews* (Vol. 34, Issue 2). https://doi.org/10.1016/j.neubiorev.2008.07.001

Fauman, M. A. (2002). *DSM-IV: Diagnostic and statistical manual of mental disorder* (1st ed.). CLIMEPSI EDITORES.

Frohlich, P. F., & Meston, C. M. (2005). Tactile sensitivity in women with sexual arousal disorder. *Archives of Sexual Behavior*, *34*(2). https://doi.org/10.1007/s10508-005-1798-6

Fuchs, A. R., Fuchs, F., Husslein, P., Soloff, M. S., & Fernström, M. J. (1982). Oxytocin receptors and human parturition: A dual role for oxytocin in the initiation of labor. *Science*, *215*(4538). https://doi.org/10.1126/science.6278592

Gastounioti, A., Hsieh, M. K., Cohen, E., Pantalone, L., Conant, E. F., & Kontos, D. (2018). Incorporating Breast Anatomy in Computational Phenotyping of Mammographic Parenchymal Patterns for Breast Cancer Risk Estimation. *Scientific Reports*, *8*(1). https://doi.org/10.1038/s41598-018-35929-9

Geer, J. H., & Fuhr, R. (1976). Cognitive factors in sexual arousal: The role of distraction. *Journal of Consulting and Clinical Psychology*, *44*(2). https://doi.org/10.1037/0022-006X.44.2.238

George, A. J., & Abraira, V. E. (2023). Good vibrations. *Science*, *381*(6660). https://doi.org/10.1126/science.adj8674

Georgiadis, J. R., Farrell, M. J., Boessen, R., Denton, D. A., Gavrilescu, M., Kortekaas, R., Renken, R. J., Hoogduin, J. M., & Egan, G. F. (2010). Dynamic subcortical blood flow during male sexual activity with ecological validity: A perfusion fMRI study. *NeuroImage*, *50*(1). https://doi.org/10.1016/j.neuroimage.2009.12.034

Georgiadis, J. R., & Kringelbach, M. L. (2016). Intimacy and the brain: Lessons from genital and sexual touch. In *Affective Touch and the Neurophysiology of CT Afferents*. https://doi.org/10.1007/978-1-4939-6418-5_18

Gonzalez, F., Brown, F. E., Gold, M. E., Walton, R. L., Shafer, B., & Mackinnon, S. E. (1993). Discussion: Preoperative and postoperative nipple-areola sensibility in patients undergoing reduction mammaplasty. *Plastic and Reconstructive Surgery*, *92*(5). https://doi.org/10.1097/00006534-199392050-00006

Greuse, M., Hamdi, M., & DeMey, A. (2001). Breast sensitivity after vertical mammaplasty. *Plastic and Reconstructive Surgery*, *107*(4). https://doi.org/10.1097/00006534-200104010-00011

Grimes, D. A., & Economy, K. E. (1995). Primary prevention of gynecologic cancers. *American Journal of Obstetrics and Gynecology*, *172*(1 PART 1). https://doi.org/10.1016/0002-9378(95)90125-6

Guérit, J. M., & Opsomer, R. J. (1991). Bit-mapped imaging of somatosensory evoked potentials after stimulation of the posterior tibial nerves and dorsal nerve of the penis / clitoris. *Electroencephalography and Clinical Neurophysiology/ Evoked Potentials*, *80*(3). https://doi.org/10.1016/0168-5597(91)90125-H

Gutiérrez-Villanueva, M., García-Mesa, Y., García-Piqueras, J., Cobo, R., García-Suárez, O., Vega, J. A., & Feito, J. (2020). The sensory innervation of the human nipple. *Annals of Anatomy*, *229*. https://doi.org/10.1016/j.aanat.2019.151456

Halata, Z., & Munger, B. L. (1986). The neuroanatomical basis for the protopathic sensibility of the human glans penis. *Brain Research*, *371*(2). https://doi.org/10.1016/0006-8993(86)90357-4

Hall, J. E. (2016). *Guyton and Hall Textbook of Medical Physiology* (13th ed.). Elsevier.

Hamdi, M., Greuse, M., DeMey, A., & Webster, M. H. C. (2001). A prospective quantitative comparison of breast sensation after superior and inferior pedicle mammaplasty. *British Journal of Plastic Surgery*, *54*(1). https://doi.org/10.1054/bjps.2000.3456

Hassiotou, F., & Geddes, D. (2013). Anatomy of the human mammary gland: Current status of knowledge. In *Clinical Anatomy* (Vol. 26, Issue 1). https://doi.org/10.1002/ca.22165

Hefter, W., Elvenes, O. P., & Lindholm, P. (2003). A retrospective quantitative assessment of breast sensation after lateral pedicle mammaplasty. *British Journal of Plastic Surgery*, *56*(7), 667–673. https://doi.org/10.1016/S0007-1226(03)00308-4

Helena Puonti. (2017). *Effects of microsurgical nerve repair on sensory function after breast reconstruction*. Faculty of Medicine, University of Helsinki.

Ho, W., Stallard, S., Doughty, J., Mallon, E., & Romics, L. (2016). Oncological outcomes and complications after volume replacement oncoplastic breast conservations—The glasgow experience. *Breast Cancer: Basic and Clinical Research*, *10*. https://doi.org/10.4137/BCBCR.S41017

Hull, E. M., & Dominguez, J. M. (2007). Sexual behavior in male rodents. *Hormones and Behavior*, *52*(1). https://doi.org/10.1016/j.yhbeh.2007.03.030

Janik, P. E., Charytonowicz, D., Miszczyk, J., & Charytonowicz, M. (2019). Female Sexual Function and Sexual Well-being Before and After Breast Reduction. *Annals of Plastic Surgery*, *82*(6), 609–613. https://doi.org/10.1097/SAP.0000000000001742

Jaspars, J. J. P., Posma, A. N., Van Immerseel, A. A. H., & Gittenberger-de Groot, A. C. (1997). The cutaneous innervation of the female breast and nipple-areola complex: Implications for surgery. *British Journal of Plastic Surgery*, *50*(4). https://doi.org/10.1016/S0007-1226(97)91155-3

Johansson, R. S., & Vallbo, A. B. (1979). Detection of tactile stimuli. Thresholds of afferent units related to psychophysical thresholds in the human hand. *The Journal of Physiology*, *297*(1). https://doi.org/10.1113/jphysiol.1979.sp013048

Kaplan, H. S. (1974). Hormones And Sex from: The New Sex Therapy,Active Treatment of Sexual Dysfunctions. *The New Sex Therapy*.

Kell, C. A., Von Kriegstein, K., Rösler, A., Kleinschmidt, A., & Laufs, H. (2005). The sensory cortical representation of the human penis: Revisiting somatotopy in the male homunculus. *Journal of Neuroscience*, *25*(25). https://doi.org/10.1523/JNEUROSCI.0712-05.2005

Kortekaas, R., Nanetti, L., Overgoor, M. L. E., de Jong, B. M., & Georgiadis, J. R. (2015). Central Somatosensory Networks Respond to a De Novo Innervated Penis: A Proof of Concept in Three Spina Bifida Patients. *Journal of Sexual Medicine*, *12*(9). https://doi.org/10.1111/jsm.12967

KRANTZ, K. E. (1958). Innervation of the human vulva and vagina; a microscopic study. *Obstetrics and Gynecology*, *12*(4), 382–396.

Krassioukov, A., & Elliott, S. (2017). Neural control and physiology of sexual function: Effect of spinal cord injury. *Topics in Spinal Cord Injury Rehabilitation*, *23*(1). https://doi.org/10.1310/sci2301-1

Krychman, M., Goren, A., Brandt, L., & McCoy, J. (2020). Novel topical formulation applied to the nipple-areola complex improves female orgasm. *Journal of Cosmetic Dermatology*, *19*(2). https://doi.org/10.1111/jocd.13262

Kühn, S., & Gallinat, J. (2011). A quantitative meta-analysis on cue-induced male sexual arousal. *Journal of Sexual Medicine*, *8*(8). https://doi.org/10.1111/j.1743-6109.2011.02322.x

Lam, R. M., von Buchholtz, L. J., Falgairolle, M., Osborne, J., Frangos, E., Servin-Vences, M. R., Nagel, M., Nguyen, M. Q., Jayabalan, M., Saade, D., Patapoutian, A., Bönnemann, C. G., Ryba, N. J. P., & Chesler, A. T. (2023). PIEZO2 and perineal

mechanosensation are essential for sexual function. *Science*, *381*(6660). https://doi.org/10.1126/science.adg0144

Laumann, E. O., Gagnon, J. H., Michael, R. T., & Michaels, S. (1994). *The Social Organization of Sexuality: Sexual Practices in the United States*. University of Chicago Press. https://doi.org/10.1177/009318539602400404

Lee, H. J., Macbeth, A. H., Pagani, J. H., & Scott Young, W. (2009). Oxytocin: The great facilitator of life. In *Progress in Neurobiology* (Vol. 88, Issue 2). https://doi.org/10.1016/j.pneurobio.2009.04.001

Lemaine, V., & Simmons, P. S. (2013). The adolescent female: Breast and reproductive embryology and anatomy. *Clinical Anatomy (New York, N.Y.)*, *26*(1), 22–28. https://doi.org/10.1002/ca.22167

Levin, R. J. (2006). The breast/nipple/areola complex and human sexuality. *Sexual and Relationship Therapy*, *21*(2), 237–249. https://doi.org/10.1080/14681990600674674

Levin, R., & Meston, C. (2006). Nipple/breast stimulation and sexual arousal in young men and women. *Journal of Sexual Medicine*, *3*(3), 450–454. https://doi.org/10.1111/j.1743-6109.2006.00230.x

Lockwood, T. E. (1991). Superficial fascial system (SFS) of the trunk and extremities: A new concept. *Plastic and Reconstructive Surgery*, *87*(6). https://doi.org/10.1097/00006534-199106000-00001

Löken, L. S., Wessberg, J., Morrison, I., McGlone, F., & Olausson, H. (2009). Coding of pleasant touch by unmyelinated afferents in humans. *Nature Neuroscience*, *12*(5). https://doi.org/10.1038/nn.2312

Longo, B., Campanale, A., & Di Pompeo, F. S. (2014). Nippleareareola complex cutaneous sensitivity: A systematic approach to classification and breast volume. *Journal of Plastic, Reconstructive and Aesthetic Surgery*, *67*(12), 1630–1636. https://doi.org/10.1016/j.bjps.2014.08.043

Losken, A., Dugal, C. S., Styblo, T. M., & Carlson, G. W. (2014). A meta-analysis comparing breast conservation therapy alone to the oncoplastic technique. *Annals of Plastic Surgery*, *72*(2). https://doi.org/10.1097/SAP.0b013e3182605598

Love, S. M., & Barsky, S. H. (2004). Anatomy of the nipple and breast ducts revisited. *Cancer*, *101*(9). https://doi.org/10.1002/cncr.20559

Macéa, J. R., & Fregnani, J. H. T. G. (2006). Anatomy of the thoracic wall, axilla and breast. In *International Journal of Morphology* (Vol. 24, Issue 4). https://doi.org/10.4067/S0717-95022006000500030

Mäkelä, J. P., Illman, M., Jousmäki, V., Numminen, J., Lehecka, M., Salenius, S., Forss, N., & Hari, R. (2003). Dorsal penile nerve stimulation elicits left-hemisphere dominant activation in the second somatosensory cortex. *Human Brain Mapping*, *18*(2). https://doi.org/10.1002/hbm.10078

Marson, L. (1995). Central nervous system neurons identified after injection of pseudorabies virus into the rat clitoris. *Neuroscience Letters*, *190*(1). https://doi.org/10.1016/0304-3940(95)11495-I

Marson, L., & Murphy, A. Z. (2006). Identification of neural circuits involved in female genital responses in the rat: A dual virus and anterograde tracing study. *American Journal of Physiology - Regulatory Integrative and Comparative Physiology*, *291*(2). https://doi.org/10.1152/ajpregu.00864.2005

Masters, W. H., & Johnson, V. E. (1966). *Human sexual response*. Little, Brown and Company.

Maughan, K. L., Heim, S. W., & Galazka, S. S. (2006). Preventing postpartum hemorrhage: Managing the third stage of labor. In *American Family Physician* (Vol. 73, Issue 6).

McNeilly, A. S., Robinson, I. C. A. F., Houston, M. J., & Howie, P. W. (1983). Release of oxytocin and prolactin in response to suckling. *British Medical Journal*, *286*(6361). https://doi.org/10.1136/bmj.286.6361.257

Morrison, I., Björnsdotter, M., & Olausson, H. (2011). Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. *Journal of Neuroscience*, *31*(26). https://doi.org/10.1523/JNEUROSCI.0397-11.2011

Murrell, T. G. C. (1991). Epidemiological and biochemical support for a theory on the cause and prevention of breast cancer. *Medical Hypotheses*, *36*(4). https://doi.org/10.1016/0306-9877(91)90018-T

Nagao, K., Tai, T., Saigo, R., Kimura, M., Ozaki, Y., Tanaka, N., Kobayashi, H., & Nakajima, K. (2014). Gaps between actual and desired sex life: Web survey of 5,665 Japanese women. In *Journal of Sex and Marital Therapy* (Vol. 40, Issue 1). https://doi.org/10.1080/0092623X.2012.691947

National Cancer Institute. (2017, February 24). *Breast Reconstruction After Mastectomy*. National Institutes of Health. https://www.cancer.gov/types/breast/reconstruction-fact-sheet

Nava, M., Quattrone, P., & Riggio, E. (1998). Focus on the Breast Fascial System: A New Approach for Inframammary Fold Reconstruction. *Plastic & Reconstructive Surgery*, *102*(4). https://doi.org/10.1097/00006534-199809040-00018

Neumann, I. D. (2008). Brain oxytocin: A key regulator of emotional and social behaviours in both females and males. In *Journal of Neuroendocrinology* (Vol. 20, Issue 6). https://doi.org/10.1111/j.1365-2826.2008.01726.x

Newcomb, P. A., & Trentham-Dietz, A. (2000). Breast feeding practices in relation to endometrial cancer risk, USA. *Cancer Causes and Control*, *11*(7). https://doi.org/10.1023/A:1008978624266

NITESCU, V. (2021). Analyzers' pathology caused by the process of biological involution (senescence) – the cause of the sexual decline of the elderly. *JOURNAL OF CLINICAL SEXOLOGY*, *3*(4). https://doi.org/10.37072/jcs.2020.04.01

Normandin, J. J., & Murphy, A. Z. (2011). Somatic genital reflexes in rats with a nod to humans: Anatomy, physiology, and the role of the social neuropeptides. *Hormones and Behavior*, *59*(5). https://doi.org/10.1016/j.yhbeh.2011.02.006

Nummenmaa, L., Suvilehto, J. T., Glerean, E., Santtila, P., & Hietanen, J. K. (2016). Topography of Human Erogenous Zones. *Archives of Sexual Behavior*, *45*(5). https://doi.org/10.1007/s10508-016-0745-z

Ogunleye, A. A., Leroux, O., Morrison, N., & Preminger, A. B. (2017). Complications After Reduction Mammaplasty. *Annals of Plastic Surgery*, *79*(1). https://doi.org/10.1097/sap.0000000000001059

Okabe, H., Hale, T. M., Kumon, H., Heaton, J. P. W., & Adams, M. A. (1999). The penis is not protected: In hypertension there are vascular changes in the penis which are similar to those in other vascular beds. *International Journal of Impotence Research*, *11*(3). https://doi.org/10.1038/sj.ijir.3900394

Okoro, S. A., Barone, C., Bohnenblust, M., & Wang, H. T. (2008). Breast reduction trend among plastic surgeons: A national survey. *Plastic and Reconstructive Surgery*, *122*(5). https://doi.org/10.1097/PRS.0b013e3181881dd7

Olausson, H., Wessberg, J., Morrison, I., McGlone, F., & Vallbo, Å. (2010). The neurophysiology of unmyelinated tactile afferents. In *Neuroscience and Biobehavioral Reviews* (Vol. 34, Issue 2). https://doi.org/10.1016/j.neubiorev.2008.09.011

PANDYA, S., & MOORE, R. G. (2011). Breast Development and Anatomy. *Clinical Obstetrics & Gynecology*, *54*(1), 91–95. https://doi.org/10.1097/GRF.0b013e318207ffe9

Penfield, W., & Rasmussen, T. (1950). *The Cerebral Cortex of Man*. The Macmillan Company.

Pfaus, J. G. (2009). Pathways of sexual desire. In *Journal of Sexual Medicine* (Vol. 6, Issue 6). https://doi.org/10.1111/j.1743-6109.2009.01309.x

Pfaus, J. G., Kippin, T. E., Coria-Avila, G. A., Gelez, H., Afonso, V. M., Ismail, N., & Parada, M. (2012). Who, what, where, when (and maybe even why)? How the experience of sexual reward connects sexual desire, preference, and performance. *Archives of Sexual Behavior*, *41*(1). https://doi.org/10.1007/s10508-012-9935-5

Rabin, R. C. (2017). After Mastectomies, an Unexpected Blow: Numb New Breasts. *The New York Times*.

Ramsay, D. T., Kent, J. C., Owens, R. A., & Hartmann, P. E. (2004). Ultrasound Imaging of Milk Ejection in the Breast of Lactating Women. *Pediatrics*, *113*(2). https://doi.org/10.1542/peds.113.2.361

Ramsay, D. T., Mitoulas, L. R., Kent, J. C., Larsson, M., & Hartmann, P. E. (2005). The use of ultrasound to characterize milk ejection in women using an electric breast pump. *Journal of Human Lactation*, *21*(4). https://doi.org/10.1177/0890334405280878

Redouté, J., Stoléru, S., Grégoire, M. C., Costes, N., Cinotti, L., Lavenne, F., Le Bars, D., Forest, M. G., & Pujol, J. F. (2000). Brain processing of visual sexual stimuli in human males. *Human Brain Mapping*, *11*(3). https://doi.org/10.1002/1097-0193(200011)11:3<162::AID-HBM30>3.0.CO;2-A

Riggio, E., Quattrone, P., & Nava, M. (2000). Anatomical study of the breast superficial fascial system: The inframammary fold unit. *European Journal of Plastic Surgery*, *23*(6). https://doi.org/10.1007/s002380000163

Robinson, V. C. (2015). Support for the hypothesis that sexual breast stimulation is an ancestral practice and a key to understanding women's health. *Medical Hypotheses*, *85*(6), 976–985. https://doi.org/10.1016/j.mehy.2015.09.002

Rowland, D. L. (1998). Penile sensitivity in men: A composite of recent findings. *Urology*, *52*(6). https://doi.org/10.1016/S0090-4295(98)00413-0

Rowland, D. L., Haensel, S. M., Koos Slob, A., & Blom, J. H. M. (1993). Penile sensitivity in men with premature ejaculation and erectile dysfunction. *Journal of Sex and Marital Therapy*, *19*(3). https://doi.org/10.1080/00926239308404903

Saeed, D., & Shousha, S. (2014). Toker cells of the nipple are commonly associated with underlying sebaceous glands but not with lactiferous ducts. *Journal of Clinical Pathology*, *67*(11). https://doi.org/10.1136/jclinpath-2014-202280

Sakuma, Y., & Pfaff, D. W. (1979). Facilitation of female reproductive behavior from mesencephalic central gray in the rat. *American Journal of Physiology - Regulatory Integrative and Comparative Physiology*, *6*(3). https://doi.org/10.1152/ajpregu.1979.237.5.r278

Sapino, G., Haselbach, D., Watfa, W., Baudoin, J., Martineau, J., Guillier, D., & di Summa, P. G. (2021). Evaluation of long-term breast shape in inferior versus superomedial pedicle reduction mammoplasty: a comparative study. *Gland Surgery*, *10*(3). https://doi.org/10.21037/gs-20-440

Sappey, M. P. C. (1874). *Anatomie, physiologie, pathologie des vaisseaux lymphatiques considérés chez l'homme et les vertébratés* (Adrien Delahaye, Ed.).

Sarhadi, N. S., Dunn, J. S., Lee, F. D., & Soutar, D. S. (1996). An anatomical study of the nerve supply of the breast, including the nipple and areola. *British Journal of Plastic Surgery*, *49*(3). https://doi.org/10.1016/S0007-1226(96)90218-0

Sarhadi, N. S., Shaw-Dunn, J., & Soutar, D. S. (1997). Nerve supply of the breast with special reference to the nipple and areola: Sir Astley Cooper revisited. In *Clinical Anatomy* (Vol. 10, Issue 4). https://doi.org/10.1002/(SICI)1098-2353(1997)10:4<283::AID-CA12>3.0.CO;2-G

Schlenz, I., Kuzbari, R., Gruber, H., & Holle, J. (2000). The sensitivity of the nipple-areola complex: An anatomic study. *Plastic and Reconstructive Surgery*, *105*(3). https://doi.org/10.1097/00006534-200003000-00012

Schlenz, I., Rigel, S., Schemper, M., & Kuzbari, R. (2005). Alteration of nipple and areola sensitivity by reduction mammaplasty: A prospective comparison of five techniques. *Plastic and Reconstructive Surgery*, *115*(3). https://doi.org/10.1097/01.PRS.0000152435.03538.43

Shih, C., Cold, C. J., & Yang, C. C. (2013). Cutaneous corpuscular receptors of the human glans clitoris: Descriptive characteristics and comparison with the glans penis. *Journal of Sexual Medicine*, *10*(7). https://doi.org/10.1111/jsm.12191

Sipski, M. L., Alexander, C. J., & Rosen, R. C. (1995). Orgasm in women with spinal cord injuries: A laboratory-based assessment. *Archives of Physical Medicine and Rehabilitation*, *76*(12). https://doi.org/10.1016/S0003-9993(95)80116-2

Slezak, S. (1993). Quantitation of sensibility in gigantomastia and alteration following reduction mammaplasty. *Plastic and Reconstructive Surgery*, *91*(7). https://doi.org/10.1097/00006534-199306000-00012

Slezak, S., McGibbon, B., & Dellon, A. L. (1992). The sensational transverse rectus abdominis musculocutaneous (TRAM) flap: Return of sensibility after TRAM breast reconstruction. *Annals of Plastic Surgery*, *28*(3). https://doi.org/10.1097/00000637-199203000-00004

Smeele, H. P., Bijkerk, E., Van Kuijk, S. M. J., Lataster, A., Van Der Hulst, R. R. W. J., & Tuinder, S. M. H. (2022). Innervation of the Female Breast and Nipple: A Systematic Review and Meta-Analysis of Anatomical Dissection Studies. *Plastic and Reconstructive Surgery*, *150*(2). https://doi.org/10.1097/PRS.0000000000009306

Spiegel, A. J., Menn, Z. K., Eldor, L., Kaufman, Y., & Dellon, A. L. (2013). Breast Reinnervation: DIEP Neurotization Using the Third Anterior Intercostal Nerve. *Plastic and Reconstructive Surgery. Global Open*, *1*(8), e72. https://doi.org/10.1097/GOX.0000000000000008

Stecco, A., Masiero, S., Macchi, V., Stecco, C., Porzionato, A., & De Caro, R. (2009). The pectoral fascia: Anatomical and histological study. *Journal of Bodywork and Movement Therapies*, *13*(3). https://doi.org/10.1016/j.jbmt.2008.04.036

Stecco, C., & Stecco, A. (2012). Fascial manipulation. In *Fascia: The Tensional Network of the Human Body* (pp. 335–342). Elsevier. https://doi.org/10.1016/B978-0-7020-3425-1.00007-6

Stone, K., & Wheeler, A. (2015). A Review of Anatomy, Physiology, and Benign Pathology of the Nipple. *Annals of Surgical Oncology*, *22*(10). https://doi.org/10.1245/s10434-015-4760-4

Tezer, M., Ozluk, Y., Sanli, O., Asoglu, O., & Kadioglu, A. (2012). Nitric oxide may mediate nipple erection. *Journal of Andrology*, *33*(5). https://doi.org/10.2164/jandrol.111.014951

The American Society for Aesthetic Plastic Surgery. (2017). *Cosmetic Surgery National Data Bank Statistics for 2017*. https://www.surgery.org/sites/default/files/ASAPS-Stats2017

Van Deventer, P. V., & Graewe, F. R. (2016). The Blood Supply of the Breast Revisited. *Plastic and Reconstructive Surgery*, *137*(5). https://doi.org/10.1097/PRS.0000000000002048

Veening, J. G., & Coolen, L. M. (1998). Neural activation following sexual behavior in the male and female rat brain. *Behavioural Brain Research*, *92*(2). https://doi.org/10.1016/S0166-4328(97)00190-3

Walker, S. C., Trotter, P. D., Swaney, W. T., Marshall, A., & Mcglone, F. P. (2017). C-tactile afferents: Cutaneous mediators of oxytocin release during affiliative tactile interactions? In *Neuropeptides* (Vol. 64). https://doi.org/10.1016/j.npep.2017.01.001

WINKELMANN, R. K. (1959). The erogenous zones: their nerve supply and its significance. *Mayo Clinic Proceedings. Mayo Clinic*, *34*(2), 39–47.

World Health Organization. (2021, February 3). *Breast cancer now most common form of cancer: WHO taking action*. https://www.who.int/news/item/03-02-2021-breast-cancer-now-most-common-form-of-cancer-who-taking-action

World Health Organization. (2024, March 13). *Breast cancer*. https://www.who.int/news-room/fact-sheets/detail/breast-cancer

Würinger, E., Mader, N., Posch, E., & Holle, J. (1998). Nerve and vessel supplying ligamentous suspension of the mammary gland. *Plastic and Reconstructive Surgery*, *101*(6). https://doi.org/10.1097/00006534-199805000-00009

Younis, I., Fattah, M., & Maamoun, M. (2016). Female hot spots. *Human Andrology*, *6*(1), 20–26. https://doi.org/10.1097/01.xha.0000481142.54302.08