

1: "indici" - Casabella - PDF Free Download

Japanese architect Shuhei Endo can be defined as an architect of steel, since he distinctly favors this material in the buildings he designs, continually experimenting with its infinite possibilities. His works are apparently weightless and communicate a sense of liberty: undulating sheets of steel.

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The architecture of Shuhei Endo and the essence of Japan / Hiroyuki Suzuki -- Paramodern architecture / Shuhei Endo -- Cyclestation M, bicycle deposit, Maihara-cho, Shiga, -- Healtecture K, home clinic, Takatsuki, Osaka, -- Transtreet Geba, park and playground, Fukui,

The Greater Tokyo Area is the most populous metropolitan area in the world. It is the seat of the Emperor of Japan and the Japanese government. Formerly known as Edo, it has been the de facto seat of government since when Shogun Tokugawa Ieyasu made the city his headquarters. It officially became the capital after Emperor Meiji moved his seat to the city from the old capital of Kyoto in ; at that time Edo was renamed Tokyo. Tokyo is often referred to as a city, but is officially known and governed as a "metropolitan prefecture", which differs from and combines elements of a city and a prefecture, a characteristic unique to Tokyo. The Tokyo metropolitan government administers the 23 Special Wards of Tokyo each governed as an individual city , which cover the area that was the City of Tokyo before it merged and became the metropolitan prefecture in . The metropolitan government also administers 39 municipalities in the western part of the prefecture and the two outlying island chains. The population of the special wards is over 9 million people, with the total population of the prefecture exceeding 13 million. The city hosts 51 of the Fortune Global companies, the highest number of any city in the world. The Michelin Guide has awarded Tokyo by far the most Michelin stars of any city in the world. Tokyo ranked first in the world in the Safe Cities Index. Tokyo hosted the Summer Olympics, the G-7 summit, the G-7 summit, and the G-7 summit, and will host the Summer Olympics and the Summer Paralympics. En el pasado, la ciudad se denominaba como Tokei, Edo o Yedo. El gentilicio de Tokio es tukiota. Le dynamique arrondissement de Shinjuku comporte de nombreux gratte-ciels, dont la mairie de la ville, et plusieurs grands magasins du Japon. Binnen deze zone woonden medio meer dan 8,7 miljoen inwoners. De totale bevolking van de prefectuur Tokio bedroeg op 1 juli meer dan 13,2 miljoen inwoners. De prefectuur Tokio vormt het centrum van de agglomeratie Groot-Tokio, de op 1 na grootste metropool van de wereld met, afhankelijk van de meetwijze, tussen de 32 en 36 miljoen inwoners. Tokio is sinds de facto de hoofdstad van Japan. De stad wordt als hoofdstad beschouwd omdat de regering er zetelt en omdat het keizerlijk paleis er staat en de Japanse keizerlijke familie er domicilie houdt. Foi fundada em , com o nome de Edo ou Yedo. . - , . , . . â€” , , .

3: USB2 - Methods and systems for leak estimation - Google Patents

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These ventilators typically comprise a source of pressurized gas which is fluidly connected to the patient through a conduit or tubing. Due to leaks and other factors, the volume of gas delivered by a ventilator system is not always the same volume of gas delivered to the lungs of the patient or exhaled by the patient. Leaks, if not accounted for, can impact triggering, cycling, and the adequacy of ventilation treatment. The internal leak or internal leak flow as used herein refers to any leak in the ventilation tubing system that occurs downstream of the proximal sensor e. The external leak or external leak flow as used herein refers to any leak in the ventilation tubing system that occurs prior to proximal sensor. The total leak or total leak flow refers to herein the air flow or volume that is input through the inspiratory module but that exits the patient tubing somewhere other than the expiratory valve and includes the internal leak and external leak. In part, this disclosure describes a method for determining leakage during delivery of gas from a ventilator to a patient via a ventilation tubing system. The proximal sensor is located at a proximate or proximal location to the patient in a patient circuit or a patient interface Yet another aspect of this disclosure describes a ventilator system including a pressure generating system, a ventilation tubing system, sensors, and an internal leak module. The pressure generating system generates a flow of breathing gas. The ventilation tubing system includes a patient interface for connecting the pressure generating system to a patient. The sensors are operatively coupled to the ventilation tubing system. The sensors include a proximal sensor and at least one of an inspiratory sensor and an expiratory sensor. The sensors generate output indicative of at least one of flow and pressure. The internal leak module estimates an internal leak flow using at least sensor output from the proximal sensor. The disclosure further describes a non-transitory computer-readable medium having computer-executable instructions executed by a processor of a controller. The controller includes an internal leak module and a total leak module. The internal leak module estimates internal leak flow based at least on sensor output from the proximal sensor. The total leak module estimates total leak flow based at least on sensor output from at least one of the inspiratory sensor and the expiratory sensor. These and various other features as well as advantages which characterize the systems and methods described herein will be apparent from a reading of the following detailed description and a review of the associated drawings. Additional features are set forth in the description which follows, and in part will be apparent from the description, or may be learned by practice of the technology. The benefits and features of the technology will be realized and attained by the structure particularly pointed out in the written description and claims hereof as well as the appended drawings. It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory and are intended to provide further explanation of the invention as claimed. A person of skill in the art will understand that the technology described in the context of a medical ventilator for human patients could be adapted for use with other systems such as ventilators for non-human patients and general gas transport systems. Medical ventilators are used to provide a breathing gas to a patient who may otherwise be unable to breathe sufficiently. In modern medical facilities, pressurized air and oxygen sources are often available from wall outlets. Accordingly, ventilators may provide pressure regulating valves or regulators connected to centralized sources of pressurized air and pressurized oxygen. The regulating valves function to regulate flow so that respiratory gas having a desired concentration of oxygen is supplied to the patient at desired pressures and rates. Ventilators capable of operating independently of external sources of pressurized air are also available. As each patient may require a different ventilation strategy, modern ventilators can be customized for the particular needs of an individual patient. For example, several different ventilator breath types have been created to provide better ventilation for patients in various different scenarios. In order to execute these different breath types and treatments accurate monitored parameters are necessary. These monitored parameters can be utilized for triggering, cycling, treatment monitoring, and etc. For example, leak

management has a significant impact on ensuring proper functioning of the ventilator as well as the adequacy of the ventilation treatment and validity of reported patient data. Leak compensation is important during ventilation because treatment delivered through patient interfaces, such as masks and endotracheal tubes are prone to experience leaks. There are known leak detection and compensation product features available for medical ventilators. However, these conventional leak detection algorithms do not differentiate between internal leak leaks occurring past the proximal sensor, e. The systems and method disclosed herein estimate the leak past the proximal sensor and proximal to the patient lungs. Accordingly, the systems and methods disclosed herein provide accurate estimates of instantaneous internal leak rates and thus enhance patient monitoring and effectiveness under time-varying pressure conditions in the presence of both rigid orifice constant size leaks as well as pressure-dependent varying-size elastic leak sources. However, these control schemes are suitable for modeling internal leak flow, which was not accounted for in prior ventilators. The present discussion will focus on specific example embodiments, though it should be appreciated that the present systems and methods are applicable to a wide variety of ventilator devices. Ventilator includes a pneumatic system also referred to as a pressure generating system for circulating breathing gases to and from patient via the ventilation tubing system, which couples the patient to the pneumatic system via an invasive e. Accordingly, the ventilation tubing system includes the patient circuit, the proximal sensor A, the patient interface, and all connections to the pneumatic system or components of the pneumatic system. The patient circuit is the tubing that connects the pneumatic system to the patient interface. Leaks occur in a variety of settings, and the disclosure contemplates that the patient interface may be invasive or non-invasive, and of any configuration suitable for communicating a flow of breathing gas from the patient circuit to an airway of the patient. The internal leak or internal leak flow as used herein refers to any leak in the ventilation tubing system that occurs downstream of the proximal sensor A. The external leak or external leak flow as used herein refers to any leak in the ventilation tubing system that occurs prior to proximal sensor A. The ventilation tubing system may be a two-limb shown or a one-limb circuit for carrying gases to and from the patient. Pneumatic system may be configured in a variety of ways. In the present example, pneumatic system includes an expiratory module coupled with the expiratory limb and an inspiratory module coupled with the inspiratory limb. Compressor or other sources of pressurized gases e. The inspiratory module is configured to deliver gases to the patient according to prescribed ventilatory settings. The ventilator may also include one or more sensors communicatively coupled to ventilator. The embodiment of FIG. Sensors may communicate with various components of ventilator, e. Sensors may employ any suitable sensory or derivative technique for monitoring one or more patient parameters or ventilator parameters associated with the ventilation of a patient. As used herein, patient parameters are any parameters determined based on measurements taken of the patient, such as heart rate, respiration rate, a blood oxygen level SpO₂, inspiratory lung flow, airway pressure, and etc. Sensors may detect changes in patient parameters. In some embodiments, a differential pressure transducer or sensor is utilized to calculate flow. Accordingly, a flow sensor as used herein includes a pressure sensor and a pressure sensor as used herein includes a flow sensor. Sensors may be placed in any suitable location, e. Further, sensors may be placed in any suitable internal location, such as, within the ventilatory circuitry or within components or modules of ventilator. In other examples, sensors may be affixed to the ventilatory tubing or may be embedded in the tubing itself. According to some embodiments, sensors may be provided at or near the lungs or diaphragm for detecting a pressure in the lungs. Any sensor located in the proximate location is referred to herein as a proximal sensor. In some embodiments, the proximate location is within 1 foot, 6 inches, or 1 inch of the patient. In alternative embodiments, the proximate location is within the patient, such as a location located within an endotracheal tube inserted in the trachea of the patient. Indeed, any sensory device useful for monitoring changes in measurable parameters during ventilatory treatment may be employed in accordance with embodiments described herein. As should be appreciated, with reference to the Equation of Motion, ventilatory parameters are highly interrelated and, according to embodiments, may be either directly or indirectly monitored. Ep is equal to respiratory elastance inverse of respiratory compliance. Rp is the respiratory resistance. Qp is the patient flow inspiratory or expiratory. Leak-compensated patient flow leak compensated Qp enables more accurate determination of respiratory

parameters and breath delivery by ventilators. The pneumatic system may include a variety of other components, including mixing modules, valves, tubing, accumulators, filters, etc. Controller is operatively coupled with pneumatic system, signal measurement and acquisition systems, sensor, display, and an operator interface that may enable an operator to interact with the ventilator. In one embodiment, the operator interface of the ventilator includes a display communicatively coupled to ventilator. Display provides various input screens, for receiving clinician input, and various display screens, for presenting useful information to the clinician. In one embodiment, the display is configured to include a graphical user interface GUI. The GUI may be an interactive display, e. Alternatively, other suitable means of communication with the ventilator may be provided, for instance by a wheel, keyboard, mouse, or other suitable interactive device. Thus, operator interface may accept commands and input through display. Display may also provide useful information in the form of various ventilatory data regarding the physical condition of a patient. The useful information may be derived by the ventilator, based on data collected by a processor or controller, and the useful information may be displayed to the clinician in the form of graphs, wave representations, pie graphs, text, or other suitable forms of graphic display. Additionally or alternatively, patient data may be communicated to a remote monitoring system or display coupled via any suitable way to the ventilator. For example, the display may display a tube or patient circuit disconnect notice based on a comparison of a ratio of total leak flow to internal leak flow to a disconnect threshold. The memory includes non-transitory, computer-readable storage media that stores software that is executed by the processor and which controls the operation of the ventilator. In an embodiment, the memory includes one or more solid-state storage devices such as flash memory chips. In an alternative embodiment, the memory may be mass storage connected to the processor through a mass storage controller not shown and a communications bus not shown. Although the description of computer-readable media contained herein refers to a solid-state storage, it should be appreciated by those skilled in the art that computer-readable storage media can be any available media that can be accessed by the processor. That is, computer-readable storage media includes non-transitory, volatile and non-volatile, removable and non-removable media implemented in any method or technology for storage of information such as computer-readable instructions, data structures, program modules or other data. Errors may be introduced due to leaks in the ventilation tubing system. The term ventilation tubing system is used herein to describe the patient circuit, any equipment attached to or used in the ventilation tubing system such as water traps, monitors, drug delivery devices, etc. Accordingly, the controller of the ventilator includes a total leak module. The total leak module of the ventilator determines or estimates the total leak flow of the ventilation tubing system. When referring to total leak in or from the ventilation tubing system, such leaks include leaks within the ventilation tubing system and leaks where the ventilation tubing system connects to the pressure generator or the patient. Thus, leaks from the ventilation tubing system include internal leak flow and an external leak flow of the ventilation tubing system. While a variety of leak estimation and leak calculation techniques may be used by the total leak module, in some embodiments leak calculation is performed in a manner similar to that described in U. Improved leak estimation may be achieved in the present examples through provision of a modeling scheme that more fully accounts for factors affecting the time-varying magnitude of leaks under interface and airway pressure variations. It has been determined that not accounting for elastic leakage from the ventilation tubing system can cause many problems.

4: Shuhei Endo : paramodern architecture - Catalog - UW-Madison Libraries

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5: Library Resource Finder: Table of Contents for: Shuhei Endo : paramodern architecture

Roofecture T, square with facilities, Fukui, Springecture H, public toilets, Shingu-cho, Hyogo, Roofecture N, office block and deposit for building materials, Nishinomiya, Hyogo,

Goldar, Institute of Economic Growth, for his guidance and support. On one hand, there are scholars who argue, using the conventional theories of trade, that trade provides opportunities by expanding markets, infusing new technologies and improving productivity, which leads to overall growth. Further, higher trade benefits low-skilled labor-intensive production, hence increasing demand and wages of low-skilled workers in developing countries; since low-skilled workers are most likely to be in a situation of poverty, there would be a reduction in poverty. Some have also argued that trade helps in poverty reduction as developing countries pursuing an export-promoting strategy will have to maintain macroeconomic stability. This reduces inflation fluctuations to which the poor are most vulnerable. Therefore greater orientation to trade encourages countries to adopt macroeconomic policies, which invariably favour the poor. On the other hand, scholars have pointed to the complexities involved in the mechanism through which trade may impact poverty. The role of specialization, intra-industry trade and perfectly elastic supply of labour has been brought to the forefront in tracing the impact of trade on poverty. It has also been argued that the trickle-down effect from growth to poverty reduction is based on the assumption that economic growth is distribution neutral, if not distribution improving, which may not be true in many cases. One extreme of the debate argues that the potential benefits of economic growth to the poor are undermined or offset by the inadequate redistributive policies and by increases in inequality that accompany economic growth. The second extreme argues that despite increased inequality, liberal economic policies and open markets raise incomes of everyone in the society including the poor. This proportionally reduces the incidence of poverty. Along with the extent of growth effects on inequality, the direction has also been debated, where it is argued that more inequitable distribution of gains lead to inequality and higher growth. Further, this debate on the trade-poverty nexus has become more complex due to the methodological issues and data limitations. In the context of the existing debates, this study How the poor are affected by international trade in India: An empirical Approach takes an alternative approach to the issue of impact of trade on poverty. Instead of estimating the net impact of trade on poverty, an attempt has been made to assess how the poor are affected by trade. The poor constitute the low income group. This approach does not attempt to arrive at the net impact of trade on poverty, since it is argued that trade may produce both winners and losers and it may not be desirable to compare the gains to losses, as losses may occur to relatively poorer section of the society and gains to relatively well-off sections or vice versa. The framework of the study involves tracing the role played by trade in influencing the four facets of human development, namely empowerment, productivity, equity and sustainability. Since these are integral parts of the millennium development goals, the study traces the role played by trade in the progress made by India in achieving these 7 8 goals. An extensive exploration is conducted in each of these issues to trace the role played by trade. Empowerment The study conducts an impact assessment to examine whether trade has empowered poor in terms of generating additional employment in the economy whereby more people are employed. Chapter 1 of the study estimates the extent of employment generated in 46 sub-sectors of the economy due to increase in exports from to The study finds that a rise in exports in the period to increased employment by 26 million person years. Results arrived at in chapters 2 and 3 show that in the unorganized sector, enterprises belonging to export-oriented industries employ more people and pay higher wages. However, it is only the relatively bigger enterprises, i. Rising import competition is found to have adversely affected employment in these enterprises. Location of an enterprise, in terms of state to which it belongs has an important bearing on the impact of trade. Irrespective to the export-orientation of the industry, unorganized enterprises in states with higher estimated export-orientation are found to gain more from exports, while impact of import competition faced by the state does not vary across states. Statistically significant results with respect to exports increasing employment in the unorganized sector are found in Andhra Pradesh, Gujarat, Haryana,, Karnataka, Maharashtra, Punjab and Tamil Nadu. Focusing on the agriculture sector,

chapter 5 and 6 of the study estimates the impact of exports and imports on wages of unskilled labour in agriculture and organized manufacturing. The results show that exports of agricultural products have not led to increase in wage rates of unskilled workers but imports of agricultural products have led to lowering of wage rates of unskilled workers in agriculture. In organized manufacturing sector, the results indicate that exports have had a favourable impact on wages of unskilled labour. Strict labour laws and downward rigidity of wages in India has perhaps prevented rising import competition from displacing unskilled labour or adversely affecting their wage rates. It has been often argued that gains from trade are not gender-neutral and women tend to gain less than men. An in-depth analysis has been undertaken to estimate the impact of trade in gender employment. The results show that increase in exports in the period to 9 generated 9. The share of females in additional employment generated due to increase in exports exceeds the share of females in total employment by nearly 5 percent points. This suggests that increase in exports have reduced the gap between male female employment in India. This result is corroborated by the estimations carried out for organized manufacturing sector, which show that export intensity has a positive and significant impact on women employment but imports have not led to any displacement of women employment. To gender sensitise trade policy in India and harness further gains from trade for women, the study has identified gender sensitive products which can be used in trade negotiations. Productivity An important aspect of trade liberalization is to induce competition so as to increase productivity levels. Studies have found that as firms are exposed to international competition through exports and domestic competition through imports, labour productivity rises. However most of the studies have been carried out for organised manufacturing sector. This study estimates the impact of trade on labour productivity in both organized as well as unorganized manufacturing sector. Further, impact of trade on labour productivity of both skilled and unskilled labour is carried out separately. The results of chapter 2 and 3 show that in the unorganized sector, export intensity of the industry to which an enterprise belongs has a significant positive impact on its labour productivity but import intensity conversely reduces labour productivity. But these effects are mainly experienced by enterprises with more than six workers. In the organized sector, the study finds that both export and import competition improves labour productivity. This has an important implication, which is, competition can have productivity enhancement effects only after an enterprise achieves a certain threshold scale of production. Higher competition, whether domestic or international, may in fact lower productivity levels of very small enterprises. Results of chapter 1 highlight an important impact of trade on productivity, which is enhancement of women skills. Exports of IT enabled services have opened new avenues of employment for women in India which has encouraged more women to upgrade their skills. The results show that higher exports of computer and communication services from India have led to higher Female Technical Education. Most of the earlier studies for India have examined this issue by comparing indicators of inequality, e. Ginni coefficients in pre and post liberalization period. This issue is approached in this study by comparing the gains from trade across different income groups and segmented labour markets. The study estimates the incomes generated due to increased exports for people in abject poverty and those below poverty line. The results of the study show that the total income generated by increase in exports in the period to has been of Rs 2, billion, equivalent to USD 55 billion. However, total income generated for the people in the lowest income group i. The results arrived in chapter 5 indicate that though exports have increased wage rates of unskilled labour, it has led to a faster rise in wages of skilled labour. This implies that exports have led to higher wage inequality between skilled and unskilled labour. Another dimension of unequal distribution of gains from trade is the gains that accrue to consumers and those which accrue to producers due to import liberalization. Consumers may gain from lower prices while producers may lose market share and their profits may shrink with higher imports. The results of the study conducted in oilseed sector indicate that the consumer gains from imports of edible oil have been high though producers have suffered a substantial loss. Sustainability Sustainability of social gains from trade is an issue of concern. Whether trade has led to social gains needs to be examined first. The causality tests show that trade has led to improvement in India's progress in achieving MDGs. The improvement in some of the development indicators has been caused by trade. Contrary to the results arrived at by other studies; this study shows that domestic prices are integrated to world prices in rice, edible oils, tea and coffee. The analysis shows that the

markets for groundnut oil, mustard oil and gram are reasonably well-integrated. Therefore, market mechanism can play a reasonably effective role in case of domestic production shocks. This study is a pioneering study in four major respects. Firstly, earlier studies on impact of trade on employment and wages have been at a disadvantage in terms of lack of trade data at industry level. Attempts were made to construct industry-level export data by aggregating firm level exports. However, many firms may not be listed firms in which case the firm-level export aggregation may have a downward bias. In case of quantifying import competition faced by an industry, lowering of tariffs have been used for indicating higher imports by most of the studies. But lowering of tariffs does not necessarily translate into higher imports, especially when domestic supply is sufficient. To address this data concern the study constructs a concordance matrix between six-digit product level data Harmonised System of Coding and three-digit industry level data National Industrial Classification. Using this concordance matrix, the exports and imports of products have been matched to the respective industries to arrive at industry level trade data. The industry level trade data is then used to estimate the impact of exports and imports on different characteristics of labour market. Secondly, the study undertakes the impact of export intensity of industries and import competition faced by the industries in the organized sector on employment, wage rate and labour productivity of enterprises in the unorganized sector. This traces an important channel through which the effects of trade can percolate to the poor. Further, the study estimates the effectiveness of the found to have a significant positive impact on the employment and wage rate in the unorganized sector. Thirdly, the study uses similar methodology to estimate the impact of trade in different sectors of the economy in the same period. The estimations for the unorganized manufacturing sector are carried out for around 83, enterprises for the year The trade data at the three digit industry level is matched to the enterprise level data using the industrial classification specified for each enterprise in NSS dataset. The estimations for the organized manufacturing sector are undertaken using a panel data for 78 industries for the period to The industry level data is extracted from Annual Survey of Industries ASI to which the trade data is matched using the concordance matrix. Similar labour demand and wage equations across sectors have been estimated. Finally, the study estimates the extent to which exports in the period to have generated employment in 46 sectors of the economy and incomes for the people in abject poverty and those below poverty line. The employment generated is also disaggregated into employment created for men and women separately. Further, impact of exports and imports on gender employment in the organized manufacturing sector has been estimated. The study makes an attempt to identify gender-sensitive products which may form a practical basis for gender sensitization of trade policy. The chapter scheme of the study is as follows: The chapter further estimates employment generated in 46 sectors of Indian economy due to rise in exports during the period to The increase in incomes across five income groups has been estimated which include people in abject poverty and those below poverty line. Chapter 2 estimates the impact of trade on labour markets in the unorganized sector. The impact on wages and employment of extent of export intensity and import competition faced by the industry to which the enterprise belongs has been highlighted. Chapter 3 undertakes the deeper analysis into tradeorientation of the state and its effect on labour markets in the unorganized sector. Chapter 4 quantifies the effects of trade on unskilled labour in agriculture and organised manufacturing industries. Chapter 5 estimates the extent to which trade has affected the wage inequality of skilled and unskilled labour and differentially affected their labour productivities.

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The disclosed methods may also be used to treat other disorders that may be co-morbid with migraine headaches, such as anxiety disorders. This application also is a Continuation in Part of U. This application also is a Continuation in Part application of U. It relates more specifically to the use of non-invasive devices, such as electrical nerve stimulation devices and magnetic stimulation devices, along with methods of treating medical disorders using energy that is delivered by such devices. The methods may also be used to treat other disorders that may be co-morbid with migraine headaches, such as anxiety disorders in which the nervous system may also be hyper-reactive and in which attacks may be triggered by some of the same factors that trigger migraine and asthma attacks. Treatments for various infirmities sometime require the destruction of otherwise healthy tissue in order to produce a beneficial effect. Malfunctioning tissue is identified and then lesioned or otherwise compromised in order to produce a beneficial outcome, rather than attempting to repair the tissue to its normal functionality. A variety of techniques and mechanisms have been designed to produce focused lesions directly in target nerve tissue, but collateral damage is inevitable. Other treatments for malfunctioning tissue can be medicinal in nature, but in many cases the patients become dependent upon artificially synthesized chemicals. In many cases, these medicinal approaches have side effects that are either unknown or quite significant. Unfortunately, the beneficial outcomes of surgery and medicines are often realized at the cost of function of other tissues, or risks of side effects. The use of electrical stimulation for treatment of medical conditions has been well known in the art for nearly two thousand years. Nerve stimulation is thought to be accomplished directly or indirectly by depolarizing a nerve membrane, causing the discharge of an action potential; or by hyperpolarization of a nerve membrane, preventing the discharge of an action potential. Such stimulation may occur after electrical energy, or also other forms of energy, are transmitted to the vicinity of a nerve [F. The basic mechanism for the electrical stimulation of the nervous system. *Neuroscience* 89 2, On soliton propagation in biomembranes and nerves. *PNAS* 28, Nerve stimulation may be measured directly as an increase, decrease, or modulation of the activity of nerve fibers, or it may be inferred from the physiological effects that follow the transmission of energy to the nerve fibers. One of the most successful applications of modern understanding of the electrophysiological relationship between muscle and nerves is the cardiac pacemaker. The first truly functional, wearable pacemaker appeared in , and in , the first fully implantable pacemaker was developed. Around this time, it was also found that electrical leads could be connected to the heart through veins, which eliminated the need to open the chest cavity and attach the lead to the heart wall. In the introduction of the lithium-iodide battery prolonged the battery life of a pacemaker from a few months to more than a decade. The modern pacemaker can treat a variety of different signaling pathologies in the cardiac muscle, and can serve as a defibrillator as well see U. Another application of electrical stimulation of nerves has been the treatment of radiating pain in the lower extremities by stimulating the sacral nerve roots at the bottom of the spinal cord see U. The principle underlying these approaches involves disruption and modulation of hyperactive neuronal circuit transmission at specific sites in the brain. Unlike potentially dangerous lesioning procedures in which aberrant portions of the brain are physically destroyed, electrical stimulation is achieved by implanting electrodes at these sites. The electrodes are used first to sense aberrant electrical signals and then to send electrical pulses to locally disrupt pathological neuronal transmission, driving it back into the normal range of activity. These electrical stimulation procedures, while invasive, are generally conducted with the patient conscious and a participant in the surgery. However, brain stimulation, and deep brain stimulation in particular, is not without some drawbacks. The procedure requires penetrating the skull, and inserting an electrode into brain matter using a catheter-shaped lead, or the like. Next, adjustments are made to the electrical stimulus signals, such as frequency, periodicity, voltage, current, etc. The electrode is then permanently implanted, and wires are directed from the electrode to the site of a surgically implanted pacemaker. The pacemaker provides the

electrical stimulus signals to the electrode to maintain the therapeutic effect. While the therapeutic results of deep brain stimulation are promising, significant complications may arise from the implantation procedure, including stroke induced by damage to surrounding tissues and the neuro-vasculature. Most of the above-mentioned applications of electrical stimulation involve the surgical implantation of electrodes within a patient. In contrast, for embodiments of the present invention, the disclosed devices and medical procedures stimulate nerves by transmitting energy to nerves and tissue non-invasively. They may offer the patient an alternative that does not involve surgery. A medical procedure is defined as being non-invasive when no break in the skin or other surface of the body, such as a wound bed is created through use of the method, and when there is no contact with an internal body cavity beyond a body orifice. Such non-invasive procedures are distinguished from invasive procedures including minimally invasive procedures in that invasive procedures do involve inserting a substance or device into or through the skin or into an internal body cavity beyond a body orifice. For example, transcutaneous electrical nerve stimulation TENS is non-invasive because it involves attaching electrodes to the surface of the skin or using a form-fitting conductive garment without breaking the skin. Potential advantages of non-invasive medical methods and devices relative to comparable invasive procedures are as follows. The patient may be more psychologically prepared to experience a procedure that is non-invasive and may therefore be more cooperative, resulting in a better outcome. Non-invasive procedures may avoid damage of biological tissues, such as that due to bleeding, infection, skin or internal organ injury, blood vessel injury, and vein or lung blood clotting. Non-invasive procedures generally present fewer problems with biocompatibility. In cases involving the attachment of electrodes, non-invasive methods have less of a tendency for breakage of leads, and the electrodes can be easily repositioned if necessary. Non-invasive methods are sometimes painless or only minimally painful and may be performed without the need for even local anesthesia. Less training may be required for use of non-invasive procedures by medical professionals. In view of the reduced risk ordinarily associated with non-invasive procedures, some such procedures may be suitable for use by the patient or family members at home or by first-responders at home or at a workplace, and the cost of non-invasive procedures may be reduced relative to comparable invasive procedures. Electrodes that are applied non-invasively to the surface of the body have a long history, including electrodes that were used to stimulate underlying nerves [L. Annals of Biomedical Engineering 25 This theory, along with advances in electronics, reawakened interest in the use of implanted electrodes to stimulate nerves, initially to control pain. Screening procedures were then developed to determine suitable candidates for electrode implantation, which involved first determining whether the patient responded when stimulated with electrodes applied to the surface of the body in the vicinity of the possible implant. It was subsequently found that the surface stimulation often controlled pain so well that there was no need to implant a stimulating electrode [Charles Burton and Donald D. Pain Suppression by Transcutaneous Electronic Stimulation. Such non-invasive transcutaneous electrical nerve stimulation TENS was then developed for treating different types of pain, including pain in a joint or lower back, cancer pain, post-operative pain, post-traumatic pain, and pain associated with labor and delivery [Steven E. Transcutaneous Electrical Nerve Stimulation. Neural stimulation Volume 2. Transcutaneous electrical nerve stimulation: Arch Phys Med Rehabil 79 A critical appraisal of the electrical output characteristics of ten transcutaneous nerve stimulators. As TENS was being developed to treat pain, non-invasive electrical stimulation using surface electrodes was simultaneously developed for additional therapeutic or diagnostic purposes, which are known collectively as electrotherapy. Neuromuscular electrical stimulation NMES stimulates normally innervated muscle in an effort to augment strength and endurance of normal e. Functional electrical stimulation FES is used to activate nerves innervating muscle affected by paralysis resulting from spinal cord injury, head injury, stroke and other neurological disorders, or muscle affected by foot drop and gait disorders. FES is also used to stimulate muscle as an orthotic substitute, e. Another application of surface electrical stimulation is chest-to-back stimulation of tissue, such as emergency defibrillation and cardiac pacing. Surface electrical stimulation has also been used to repair tissue, by increasing circulation through vasodilation, by controlling edema, by healing wounds, and by inducing bone growth. Surface electrical stimulation is also used for iontophoresis, in which electrical currents drive electrically charged drugs or other

ions into the skin, usually to treat inflammation and pain, arthritis, wounds or scars. Stimulation with surface electrodes is also used to evoke a response for diagnostic purposes, for example in peripheral nerve stimulation PNS that evaluates the ability of motor and sensory nerves to conduct and produce reflexes. Surface electrical stimulation is also used in electroconvulsive therapy to treat psychiatric disorders; electroanesthesia, for example, to prevent pain from dental procedures; and electrotactile speech processing to convert sound into tactile sensation for the hearing impaired. All of the above-mentioned applications of surface electrode stimulation are intended not to damage the patient, but if higher currents are used with special electrodes, electrosurgery may be performed as a means to cut, coagulate, desiccate, or fulgurate tissue [Mark R. The effects of electric current applied to skin: A review for transdermal drug delivery. *Advanced Drug Delivery Reviews* 18]. Despite its attractiveness, non-invasive electrical stimulation of a nerve is not always possible or practical. This is primarily because the current state of the art may not be able to stimulate a deep nerve selectively or without producing excessive pain, since the stimulation may unintentionally stimulate nerves other than the nerve of interest, including nerves that cause pain. For this reason, forms of electrical stimulation other than TENS may be best suited for the treatment of particular types of pain [Paul F. *Anesth Analg* 92]. For some other electrotherapeutic applications, it has also been difficult to perform non-invasive stimulation of a nerve, in lieu of stimulating that nerve invasively. The therapies most relevant to the present invention involve electrical stimulation of the vagus nerve in the neck, which was developed initially for the treatment of epilepsy. The left vagus nerve is ordinarily stimulated at a location within the neck by first surgically implanting an electrode there, then connecting the electrode to an electrical stimulator [U. Deep brain stimulation, vagal nerve stimulation and transcranial stimulation: An overview of stimulation parameters and neurotransmitter release. *Neurosci Biobehav Rev Neurosurg Focus* 25 3]. When it is desired to avoid the surgical implantation of an electrode, vagal nerve stimulation VNS may be performed less invasively by positioning one or more electrodes in the esophagus, trachea, or jugular vein, but with one electrode positioned on the surface of the body [U. Despite their advantage as being non-surgical, such methods nevertheless exhibit other disadvantages associated with invasive procedures. In other patents, non-invasive VNS is disclosed, but at a location other than in the neck [e. However, because such non-invasive VNS occurs at a location other than the neck, it is not directly comparable to invasive VNS in the neck, for which therapeutic results are well documented. Among other patents and patent applications, non-invasive VNS is sometimes mentioned along with invasive VNS methods, but without addressing the problem of unintentional stimulation of nerves other than the vagus nerve, particularly nerves that cause pain [e. Other patents are vague as to how non-invasive electrical stimulation in the vicinity of the vagus nerve in the neck is to be accomplished [e. The present invention uses electrical nerve stimulation to treat headaches, particularly non-invasive vagal nerve stimulation in the neck. The present invention is particularly suitable for the treatment of migraine and cluster headaches, as well as disorders with which those headaches are co-morbid. According to the ICHD-II, migraine is not a homogenous entity, but is instead a group of syndromes, some categories of which are distinguished by the presence of an aura that usually occurs shortly before pain of the headache. The aura typically lasts for 5 minutes to an hour, during which time the patient experiences sensations such as moving zig-zag flashes of light, blind spots or tingling in the hand or face. The features most predictive of the diagnosis of migraine, rather than tension-type headaches, are nausea, photophobia, phonophobia, exacerbation by physical activity and aura. The duration of pain is of little differential diagnostic value for discriminating migraine from tension and other types of headache. It occurs in all age groups but reaches a peak in middle age. Migraine headaches often occur on both sides of the head in children, but an adult pattern of unilateral pain often emerges in adolescence.

7: USB2 - Methods and devices for treating primary headache - Google Patents

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