Original Article

Conception, Development, and Clinical Trial Design of Point-of-care Technologies: A Case of Improved FES Device Development

C V Shendkar[1], Bikas K Arya[2], PK Lenka[3], Ratnesh Kumar[4], Abhishek Biswas[5], Mahadevappa M[6]

Abstract

Objective: This article presents a case study on the development of an indigenous stimulator device, including the design of its clinical trials and the process of its clinical trial registration in the newly launched clinical trial registry-India (CTRI). The ethical and regulatory issues involved in medical device clinical trials in India are also discussed.

Design and Methods: The entire development and trial cycle of a new medical device from ideation to technology transfer is explained in this case of a newly developed indigenous FES device. The primary emphasis is on how to systematically analyse the global trial registry databases to adequately frame a medical device trial. With this case study, we present how to shortlist relevant trials; we then compare them and explain the valid methods for registering a trial protocol in the CTRI.

Conclusions: Our work can act as a model or guide for rehabilitation researchers in India, facilitating there work in the medical device design and trial protocol development. Though our trial has been designed for and registered in the Indian CTRI trial registry, our work can be equally useful for researchers abroad who desire to conduct their medical device trials in India.

Key words: **Clinical Trial Registry-India (CTRI), functional electrical stimulation, stroke rehabilitation, medical device design, medical device clinical trial protocol design, neuromuscular electrical stimulation.**

Introduction:

Before the launch of a newly developed medical device, its successful clinical trial is mandatory. A clinical trial is a controlled experiment in human subjects. Medical device trials determine whether the intervention provided through the use of the device is safe and effective. We present here a case study of an entire device development cycle and our experiences with the requirements dictating the development, design, registration and conduct of the clinical trial of a functional electrical stimulation (FES) device. An FES device is a medical device used to induce therapeutic and orthotic effects in stroke survivors. This device has been developed to meet the local population's requirements by incorporating appropriate technological advancements. After the device's development, we focused on its clinical trial, and the clinical trial protocol for the indigenously developed FES device was subsequently designed and registered in the Clinical Trial Registry- India (CTRI).

All clinical trials require registration in the clinical trials registry (CTR) and must follow the rules of various regulatory authorities. The primary purpose of the CTR is to remove trial data publication bias. The largest and most widely used CTR is that of the United States National Library of Medicine (NLM), which is hosted at the clinical Trials.gov portal[1]. In India, the CTRI is the Indian government's initiative for an online public record system for the registration of clinical trials being conducted in India[2].

Authors' affiliation:

[1] *PhD Student, M.Tech.*
[2] *PhD Student, MMST.*
[3] *PhD.*
[4] *MBBS, D Ortho, MS, DNB.*
[5] *MBBS, MD.*
[6] *PhD.*
Department of PMR NIOH Kolkata and IIT Kharagpur

Cite as:

C V Shendkar, Bikas K Arya, PK Lenka, Ratnesh Kumar, Abhishek Biswas, Mahadevappa M. Conception, development, and clinical trial design of Point-of-Care Technologies: A case of improved FES device development. IJPMR, March 2016; Vol 27(1) :2-9

Correspondence:

Mahadevappa M, School Of Medical Science and Technology, Indian Institute of Technology (IIT), Kharagpur. West Bengal, India-721 302. E-mail: mmaha2@smst.iitkgp.ernet.in ; mmaha2@gmail.com, Phone: +91-3222-282300,Fax: +91-3222-282221

Received on 14/01/2014, Accepted on, 01/01/2016

A new medical device should go through the developmental phases of identifying the users' requirements, technical design, fabrication, clinical trial design, conducting the clinical trial, and ultimately, technology transfer. For successful technology transfer to occur, not only correctly identifying the users' needs but also adopting an integrated development platform and validating the device by a well-designed clinical trial is most important. There is a lack of research articles or case studies that explain in a systematic manner how to proceed in designing and registering a new device in trial registries. For example, in India since June 15, 2009, the government has made it mandatory to register a clinical trial involving human participants; since then, a total of 4379 clinical trials have been registered in the CTRI, but case studies on device clinical trial design, trial registration and regulatory aspects are lacking. Also, there are no articles or case studies to teach international researchers about the device trial procedure and the Indian regulatory environment concerning medical devices.

This article presents the entire device development process from the ideation stage to the trial's design and its registration in a manner that will help new device developers to align their work with industries' requirements for technology transfers. In our device trial design case study, we present a systematic approach towards a robust trial design for a new device by using information from an existing trial registry. The trial protocol and trial registration process presented in this paper will be useful to researchers focusing on new device trial design.

Materials and Methods and Results:

In this section, we discuss the background work needed for a clinical trial of any point-of-care technology. The content of this section will become clearer to the reader later on during consideration of the FES case study that is described as an example. The entire process can be divided into four main tasks i.e, (I) Need identification and conception; (II) development and testing of proposed device; (III) trial of device developed after relevant approval and regulatory consideration; (IV) technology transfer issues. We have intentionally focused on the first 3 tasks, as we are in the final phase of the trial and data analysis currently being conducted. However, that final task is presented in this paper as a future work. An overview of the entire processes involved is briefly illustrated in Fig1.

Fig 1- Conception, Development, and Clinical Trial of Point-of-care Technologies: A Case of Improved FES Device Development for the Indian Population

A. TASK 1: Need Identification and Conception

The annual incidence of stroke in India amounts to nearly 1 million cases per annum[3]. In this context, the work of our colleagues[4] was significant for us, as their study conducted a preliminary observational study, workflow analysis of stroke care and discussion/ feedback from various stakeholders (from patient, caretakers, health workers, etc) and recommended a tele-medical solution, computerised decision support and rehabilitation technologies to improve stroke care in the present Indian scenario. Rehabilitation services are not readily available to the majority of the population in India[5,6]. Our intention to work on stroke rehabilitation has the potential to benefit a large population. In our independent analysis, after discussions with clinicians at the National Institute of Orthopaedically Handicapped (NIOH) at Kolkata, we found that very limited options (like conventional physiotherapy) are available for the rehabilitation of stroke survivors in India. The recent literature on advances in stroke rehabilitation and the National Health Science (NHS-UK) guidelines on neurological disorders recommend the use of FES in correcting the problem of foot drop[7]. The operating cost is the most important determinant for this rehabilitation technology from the perspective of the population of developing countries. Therefore, we focused our research on the development of an indigenous low-cost FES device.

Table 1: *Comparison of Fields in CTRI and Shift Clinicaltrial.gov*

Sr No	Clinical Trial Registry – India (CTRI) Descriptors	Clinicaltrial.gov Descriptors
1	CTRI number	NCT number
2	Last modified on	Last updated date
3	Type of study	Study type
4	Type of trial	Study design
5	Study design	…….
6	Public title	Brief title
7	Measure scientific title	Official title
8	Secondary IDs	Other study ID numbers
9	Principal investigators name and address.	Investigators
10	Contact person for scientific query	Contacts
11	Contact person for public query	…….
12	Sources of monetary support	…….
13	Primary sponsor	Sponsors
14	Secondary sponsor	Collaborators
15	Detailed description countries of recruitment	Location countries
16	Ethical Committee details and ethical approval status	Responsible party
17	Regulatory clearance from DCGI.	Data monitoring committee
18	Health condition/ Problem study	Condition
19	Intervention/ Comparator agent	Intervention
20	Comparator agent	Study arms
21	Inclusion criteria	Inclusion criteria
22	Exclusion criteria	Exclusion criteria
23	Random sequence generating method	…….
24	Publications method of concealment	…….
25	Blinding or masking	…….
26	Primary outcomes	Current/Original primary outcome measures
27	Secondary outcomes	Current /Original secondary outcome
28	Target sample size	Estimated enrolment
29	Phase of trial	Study phase
30	Date of first enrolment	Start date
31	Estimated duration of trial	Estimated primary completion date
32	Recruitment status of trial	Recruitment status
33	Brief summary	Brief summary
34	References	Publications

Before starting, we performed a preliminary search of the regulatory requirements, related patents and available products on the market to direct ourselves towards a potential need-based feasible conception of device design. We searched Indian patents using the freely available iPairs (Indian Patent Information Retrieval System)[8]. The search yielded only 5 results for stimulator devices, and none of them were used for stroke survivors' rehabilitation. A low-cost device meets the requirements of various stakeholders, such as the state department for rehabilitation and state-run orthopaedic and rehabilitation facilities. The FES appears to be a good fit for business models in industry, in view of its potential demand in the vast Indian market.

B. TASK 2: Development and Testing of Proposed Device

At this stage, we affirmed the need for an improved, low-cost, indigenous stroke rehabilitation device for correcting foot drop. After discussing the requirements with stakeholders and comparing the specifications of existing devices, we proposed the following modification in the design of a new FES device to make it more suitable for Indian patients.

(1) Using only one rotary knob for the adjustment of the most important stimulation parameters instead of sophisticated graphical user interface.

(2) The auto-adjustment of the stimulation parameters based on the electromyogram of the contralateral limb.

(3) In older age, locomotor activity is more important than the fine muscular activity of the hand[9]. Therefore, a low-cost single-channel foot drop stimulator design for foot drop correction was considered to be a priority over a multichannel hand-grasp stimulator.

(4) From the perspective of a developing countries' population, the primary issue in current FES technology is its high operating cost (the battery requires frequent replacement).

(5) Another important issue is the fatigue of the stimulated muscle that is produced by existing devices due to their charge unbalanced pulses.

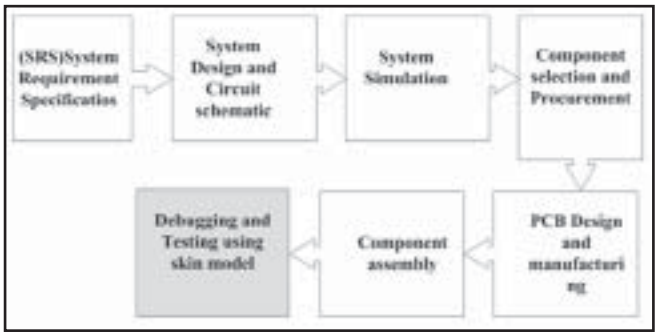
We have attempted to resolve these issues in designing the FES device using DC-DC booster technology, which produces charge-balance waveforms, causes less muscle fatigue and consumes less power. We proposed a DC booster-based single-channel electromyogram (EMG) controlled FES design for better acceptance of the FES device for home-based care in the Indian population. Our goal was to prove the feasibility of the concept. Finally, the system requirement specifications (SRS) were listed to design the entire device (Fig 2). The details of the system design, circuit schematics, system simulation, components and assembly are reported elsewhere (under review). After the development of the device, we focused on the research question of whether this low-cost indigenous device was as efficacious as the other commercially available approved products.

Table 2: *Selected Features of Shortlisted Trial Found Relevant for Designing Our Trial Protocol*

Trial No	Device Used	Inclusion criteria	Exclusion Criteria	Study Design	Imp Outcome measures	Intervention Model Study arms	Relevant comment
NCT01138995	NESS L 300	Age>18 yrs., inadequate dorsiflexion/ limb clearance	Used of any FES device	SB-RZ	10 m walking, Fall rate, BBS	Crossover assignment, AFO vs. FES	Kinematic parameters measurements used, multisite study for 42 weeks (long use)
NCT00148343	ODFS	18 < Age <80 yrs. Also considers those using AFO	Absent sensation of the affected lower limb	B-RZ	FMA, Gait Analysis	Parallel assignment, FES vs. AFO for 12 weeks only	Carry-over effect investigated by 36 weeks follow-up
NCT01087957	Walk Aide	Age>18 yrs., H/O stroke >6 months, initial gait speed < 0.8 m/s	Participation in another clinical trial, life expectancy less than 12 months	NB-RZ	Increase in gait velocity, adverse events	Parallel assignment, FES vs. AFO	Adverse event studied
NCT00552916	Compex Motion	Age>65 yrs., H/O stroke >12 months	Ability to walk more than 10 meters during a two minute walk	SB -RZ	Improvement of walking ability on a two-minute walk test	Parallel assignment FES vs. Sham	Dichotomous outcome (i.e., yes/ no about walking improvement) used
NCT01257646	Gait analysis	20 < Age <75, Ability to walk 10 m with or without a cane	Patient is not covered by a social security system	observational study	Timing of heel strike (s)	Recent stroke group (>6 month), Old stroke (>1 year)	No FES, GAIT analysis, and EMG used
NCT00991406	EMS 2000	Age>18 yrs., physical assistance or other assistive aid allowed	Ankle plantar flexor contraction	NB-NZ	Walking stability and speed	Single Group Assignment	Optimal patterns of stimulation investigated
CTRI/2012/09/ 003019 [Trial registered by Authors]	NIOH-IIT v1.0	21 < Age <65 yrs., unable to achieve normal heel strike on ambulation	Patients with leg having regional disorder, fracture or dislocation	NB-NZ-Multi arm	Quantitative Gait Analysis, sEMG changes, ROM, FMA, MAS, EEG, blood flow	Multi-arm assignment with 2 comparators, imported FES vs. physiot herapy vs. indigenous FES	Device safety, efficacy as compare to existing device, mechanism underlying improvement due to FES by kinesiology evaluation studied

(Abbreviations: B- Blinded, NB- Non - blinded, RZ- Randomised, SB- Single blinded, AFO- Ankle foot orthothosis, FMA- Fugal Meyer assessment, MAS- Modified Ashworth scale, ROM- Range of motion, H/O- History of, sEMG- Surface electromyogram, EEG- Electroencephalogram, BBS- Berge balance score)

Fig 2 - Overview of the Device Designed from SRS to Debugging and Testing



C. TASK 3: Device Trial Developed

We realised that there were multiple questions regarding the regulation of medical device trials and clinical trials in India. In this section, we present a case study on how we designed the protocol for the clinical trial of our FES device and registered it in the CTRI.

Trial registration became mandatory because some researchers in the past had not published unfavourable trial results or had published only some of the results after modifying the pre-specified hypothesis. This creates publication bias and outcome reporting bias. The primary aim of CTR is to prevent this bias. CTR information is also useful to the others conducting trials or to ethics committees to learn how much research is already underway in a specific field. Nevertheless, the CTR is not responsible for the scientific quality of a trial.

(I) Survey of standard medical journals and trials registered in CTR (Phase I)

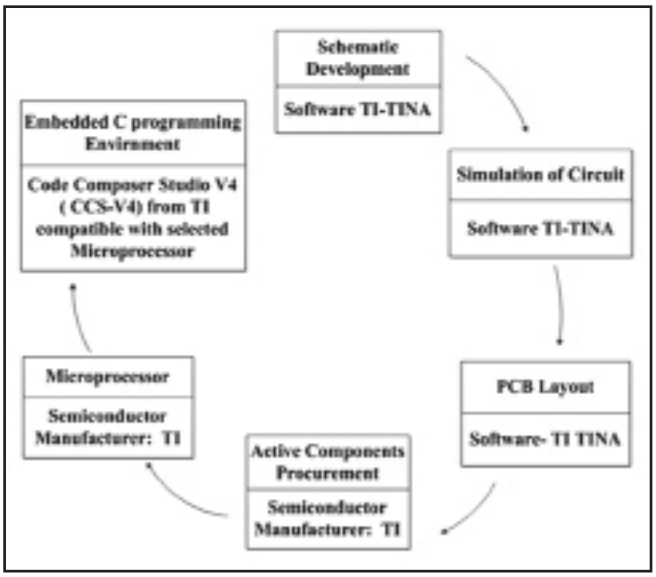
We used the Cochrane database of systematic reviews, the Cochrane Library[10], and the guidelines of the National Health Service (NHS) on FES in the initial stage of protocol design to search for studies of similar devices. After a basic literature review, we searched numerous databases for published trials, including PubMed, using the appropriate key words related to electrical stimulation in stroke rehabilitation.

After searching the conventional literature in the initial phase, we moved to searching the trial registry databases. First, we used the specific medical condition and intervention to locate relevant trials in the 'ClinicalTrials.gov' registry. We used the WHO, CTRI, and clinicaltrial.gov to find registered trials. During the course of our search, we discovered that the fields used in the databases of the Indian registry differ from those of US or European databases. Some of these fields were specifically related to the hypothesis being tested, ethical clearance details, a summary and infrastructure availability, etc. Discrepancies between the fields used should be known to the protocol designer a priori. Table 1 shows the standard data field items for the CRT[12].

(II) Selection of trials (Phase II)

We tabulated the trials, listing registration number, title, condition (health type), study type, interventions, study design, and outcome measures. Trials that were relevant to our work were shortlisted on the basis of invasiveness (if the stimulator device used is invasive or non-invasive), trial type, intervention, health condition and comparator agent. We found that the results of a trial search heavily depend on the key words provided and the nomenclature used for interventions in the searched results.

Fig 3 - Process of Device Design. An Integrated Platform Was Used at All Stages of the Device's Development



A sample draft provided by the CTRI website describes each field and its corresponding descriptor. We used this draft for structuring our clinical trial. As we had searched for all clinical trials related to FES irrespective of the country of origin, it was necessary to differentiate the fields of clinicaltrial.gov (USA) and the CTRI (India). We compared the study fields of the clinical trial registry of India with those of clinicaltrial.gov. We had selected 6 important fields from 20 clinicaltrial.gov fields and 34 CTRI fields, based on which we compared the shortlisted trials. These fields are the device used, inclusion criteria, exclusion criteria, study design, important outcome measures, intervention model and study arms, as shown in Table 2. This table does not fully depict all of the inclusion or exclusion criteria or other field details; rather, it gives only specific or important points and excludes the less important details.

- Summary of key findings from the shortlisted trials:

Most of the shortlisted clinical trials were specifically aimed at evaluating the efficacy of FES devices. An improvement in walking speed was used as the primary assessment parameter for the evaluation of performance. Commonly observed secondary outcome parameters were the BBS, MAS, and FMA scores. The studies focused on FES *versus* AFO performance testing (Table 2 for a list of abbreviations)[2]. One study conducted 42 weeks (long use) of follow-up, while another aimed at evaluating carry-over effects. Most of the inclusion criteria were considered, with a higher upper age limit up to 80 years.

(III) Designing the protocol for the proposed trial (Phase III)

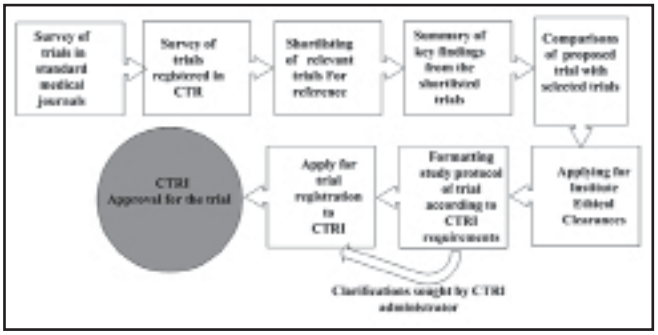
- Aim of our trial design:

We designed a multi-arm controlled clinical trial oriented towards three goals. The first was to evaluate the kinesiological and physiological changes caused by the FES. The second aim was to perform safety and efficacy evaluations of an indigenous low-cost FES design, with the specific target of observing a new intervention rehabilitation strategy in a typical Indian setting. The third goal was to analyse power consumption and muscle fatigue caused by stimulation.

- Detailed comparison of our proposed trial with selected other trials:

The clinical trial design of the proposed study is a multi-arm, non-randomised controlled trial. The three arms in the study are (i) the intervention arm using the indigenous FES device. (ii) the comparator arm using physiotherapy (iii) and the comparator arm using intervention with a CE-approved imported FES device. The duration for the intervention is set at 12 weeks. The efficacy was related to the selected outcomes of changes in the kinematic and kinesiological parameters (Gait, sEMG, ROM, FMA, MAS, EEG- Table 2 for abbreviation)[2]. Other aspects evaluated included the power consumption of the device and the fatigue time of the stimulated muscles. Our study differs from existing trials in three features: (i) we are comparing an existing CE-approved device with an indigenous low-cost FES device developed by our team for its efficacy and safety, (ii) physiotherapy is used as the comparator agent rather than AFO, which is commonly used in other studies, and (iii) the outcome measures are chosen such that they will underpin unpin the efficacy of our device for FES therapy.

Fig 4 - Process of the Protocol's Design and Registration in Clinical Trial Registry – India



(IV)Approval and Clearances (Phase IV)

- Collaborator and sponsor:

Any device trial needs appropriate funding to ensure the smooth functioning of the processes. This work was supported by the NIOH-Kolkata under the Ministry of Social Justice and Empowerment, Goverment of India. NIOH Kolkata was the clinical site of the study.

- Institute Ethical Clearances:

Ethical clearances from all of the collaborating institution's review boards were received. We primarily referred to the US and an Indian clinical trial registry while designing the trial protocol and a detailed document was presented to the ethics clearance committee. The modifications suggested by the ethics approval committee were also incorporated.

- CTRI requirement for prospective registration of clinical trials:

Once the protocol is ready according to the guidelines, we are expected to submit the proposal as per the sample template provided by the CTRI. The proposal should be accompanied by an ethical clearance letter, ethics committee details and a letter of clearance from the Drug Controller General of India (if needed) before submitting it to the CTRI. After a preliminary review and clarifications, the CTRI administrator generates a trial number[2].

- Current status of our trial :

Our trial has been registered in the CTRI under the number CTRI/2012/09/003019. The trial details are accessible both from the WHO's search portal for the International Clinical Trials Registry Platform (ICTRP) as well as from the CTRI. We have completed the process of the device's development and are in the completion mode of the device's clinical trial. Partial trial results have been communicated to the 'Hong Kong Journal for Physiotherapy'. As soon as the trial is closed, the full results will also be published in the trial registry.

D. TASK 4: Technology Transfer and Marketing Strategies (possible future work)

To facilitate the ease of technology transfer, we procured the components from standard semiconductor chip manufacturers. Fig 3 shows the schematics of the device design process. Common compatible platforms from Texas Instrumentation (TI) were used for both the software and the hardware. TI-TINA software was used for the schematic development, simulation of circuits, and PCB layout. The active components and microprocessors used were obtained from TI. We believe that using a uniform platform as required by the industry standards at the beginning stages of device design facilitates the easy percolation of point-of-care technologies into industry.

Once the trial of the device is complete and a manufacturer is identified, one should be aware of the regulatory guidelines for marketing the products. In the United States, the CDRH (Center for Devices and Radiological Health) under the US Food and Drug Administration (FDA) is responsible for the review and approval of medical devices through its office of device evaluation (ODE). Depending upon the classification of the device, the FDA's approval of the device may take 1 of 3 possible pathways: (i) Exemption, if the risk involved is insignificant; (ii) clearance, based on the similarity to an existing approved device (510k pathway); or (iii) premarketing approval (PMA), for those not falling under the above two categories. Typically, initiating a clinical trial institute review board (IRB) clearance is sufficient, but one may also seek investigational device exemption.

Table 3: *Authorities Regulating Medical Devices in Different Countries*

Country	Medical Devices Regulatory Authority
US	Center for Devices and Radiological Health under US Food and Drug Administration (FDA)
Europe	CE marking process implemented through "notified bodies" under Medical Devices Directive (MDD).
Canada	Health Canada's Therapeutic Products Directorate
Australia	Therapeutic Goods Administration (TGA) under department of Health and Aging
Japan	Ministry of Health, Labor, and Welfare (MHLW) and Pharmaceutical and Medical Device Agency (PM DA)
Brazil	The Brazilian National Health Surveillance Agency (ANVISA) under Ministry of Health (MOH)
Russia	Ministry of Health and State Committee for Standardization, Metrology and Certification (Gosstandart)
India	Central Drug Standards Control Organization (CDSCO) within the Ministry of Health
China	State Food and Drug Administration (SFDA)

Presently, no specific agency exists in India that is dedicated to regulating medical devices[11]. Since 2006, ten medical devices have been classified as a "notified medical device" and are treated as "drugs" for regulatory approval under the Drugs and Cosmetics Act. The Central Drug Standards Control Organisation (CDSCO) within the Ministry of Health is responsible for such approval. The lack of explicit guidelines in India has opened a simple route to a large market for the medical device industry. Our FES device does not fall under the category of a notified medical device and can be freely marketed in India. The details of the regulatory process can be viewed on the website of the concerned regulatory bodies (Table 3)[12].

Discussion and Conclusions :

This work contains a case study of a new medical device design, its clinical trial design and its registration in the CTR. The development of a clinical trial protocol is a cyclic process (Fig 4). Though the scientific questions are inspired by either biological or logical plausibility, protocol design largely depends on the availability of resources and the ethical aspects. Ethical obligations limit the repetition of studies. Under such circumstances, designing the optimum protocol for a clinical trial is as important as the development of the device. Hence, one of primary focuses of this paper was on the protocol's development.

The design of a trial, the manner conducting it and the reporting of the results at the end of the clinical trial should be conducted in a structured manner to maintain the gold standard and the simplicity of evaluating the method of intervention[13,14]. However, clinical trials may yield biased results if they lack methodological rigor. The current article attempts to suggest a framework for the development of point-of-care technologies for medical device innovators. The focus of our description was on India; however, we have referred to almost all of the major guidelines in our consideration of the global perspective[12]. A trial registry is an important platform for disseminating all of the information on currently running trials before their results are actually published. Not all trial results are published. This happens particularly when trials are industry driven and industry sponsored. Negative results are often not reported[15]. Under these circumstances, the registration of a trial before the trial actually starts helps other researchers use caution in selecting the problem statement and the direction of the device's design. An official survey found that the reporting quality of randomised controlled trials (RCTs) had improved in Indian journals since the mandatory registration of clinical trials in the CTRI[15,16]. The CTRI template facilitates the reporting of valid methods in registered trial protocols. The reporting of ethical issues and study methods has also improved significantly due to CTRI's recommended protocols.

Different countries have different regulatory frameworks. We have described our experience in trial registration with the CTRI. One point to be noted is that we designed this trial by comparing different trial registries across the globe, and the CTRI registry is very similar to those registries. Hence, this work can be useful for a robust trial design that is intended to be registered in any country. Additionally, researchers whose device trials have already been conducted in their home country and who intend to conduct device trials in India will benefit from our work. Thus, even though sections of this article discuss the Indian regulatory context, it has universal appeal. We followed international standards and considered India's requirements while designing this new medical device and its clinical trial design and CTRI registration. Our trial's details are also available at the WHO site, as the CTRI is an approved trial registry for an international audience. This case study thus can be useful for international research groups who want to conduct their device trials in India.

With this device case study, we emphasised correctly identifying needs, the use of an integrated development platform in the technical design, a systematic trial design approach, its registration in CTR and the resolution of regulatory issues for the successful technology transfer of medical device. We have not provided the technical engineering design details but have presented a case study for a new device from conceiving the idea to the trial of the device. An article on the detailed design will be published elsewhere. Partial results of the trial have been communicated to the 'Hong Kong Journal for Physiotherapy'. As soon as the trial is closed, full results will be published in the trial registry. We foresee that our experience in device trial design and registration will be helpful for our peers who intend to follow a similar path in device research.

What We Already Knew And What We Learn From This Article :

The process of designing and development of new medical and clinical trial of it is well established in developed countries. In India since June 15, 2009, the

government has made it mandatory to register a clinical trial involving human participants; since then, a total of 4379 clinical trials have been registered in the CTRI, but case studies on device clinical trial design, trial registration and regulatory aspects are lacking. Also, there are no articles or case studies to teach international researchers about the device trial procedure and the Indian regulatory environment concerning medical devices. With our experience of development of stroke rehabilitation device (FES device) we have explained the all aspects regarding conception, development, and clinical trial design of point-of-care rehabilitation technologies to make it a tested, safe and successful medical device ready for the rehabilitation engineering industry.

Acknowledgements:

The authors thank Avhihit Kumar for conceiving of the proposed trial outline.

Conflicts of Interest:

The authors declare that there are no conflicts of interest.

References:

1. http://clinicaltrials.gov/ (accessed on Aug 1, 2012).
2. Shendkar C, Arya BK, Lenka PK, Kumar R, Mahadevappa M. CTRI registration and protocol designing for clinical trial of medical devices: a case of FES device for foot drop. 2013; Int. conf. on Point-of-Care Healthcare Technologies (PHT), EMB-IEEE : 275-278.
3. Banerjee TK, Das SK. Epidemiology of stroke in India. *Neurol Asia* 2006; **11:** 1-4.
4. Rishi Raj KMH, Das Bhattacharya S. Stroke informatics. Postgraduate Thesis vol. Sch. Med. Sci. & Tech., IIT Kharagpur, Kharagpur, India. 2011-2012.
5. Beattie PF, Pinto MB, Nelson MK, Nelson R. Patient satisfaction with outpatient physical therapy: instrument validation. *Phys Ther* 2002; **82:** 557-65.
6. Taylor FC, Kumar S. Stroke In India Factsheet (updated 2012).
7. Shiels J, Wilkie K, Bulley C, Smith S, Salisbury L. A mixed methods service evaluation of a pilot functional electrical stimulation clinic for the correction of dropped foot in patients with chronic stroke. *Prim Health Care Res Dev* 2011; **12:** 187-99.
8. http://www.ipindia.nic.in/ (accessed on10 January 2011).
9. Mollentze W. Management of diabetes in the elderly. *Continuing Med Educ* 2010; **28:** 480.
10. Pomeroy V, King L, Pollock A, Baily-Hallam A, Langhorne P. Electrostimulation for promoting recovery of movement or functional ability after stroke. *Cochrane Database Syst Rev* 2006; **37:** 2441-2.
11. Jayaraman K. Outsourcing clinical trials to India rash and risky, critics warn. *Natl Med J* 2004; **10:** 440-4.
12. Zenios SA, Makower J, Yock PG, Brinton TJ, Kumar UN, Denend L, *et al*. Biodesign: the process of innovating medical technologies. Cambridge: Cambridge University Press, 2010.
13. Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, *et al*. The revised CONSORT statement for reporting randomised trials: explanation and elaboration. *Ann Int Med* 2001; **134:** 663-94.
14. Tharyan P, George AT, Kirubakaran R, Barnabas JP. Reporting of methods was better in the Clinical Trials Registry-India than in Indian journal publications. *J Clin Epidemiol* 2012; **661:** 10-22.
15. Tharyan P. Ethics committees and clinical trials registration in India: opportunities, obligations, challenges and solutions. *Indian J Med Ethics*2007; **4:** 168-9.
16. Pandey A, Aggarwal A, Seth S, Maulik M, Bano R, Juneja A. Clinical Trials Registry-India: Redefining the conduct of clinical trials. *Indian J Cancer* 2008; **45:** 79.