



# NeuroMaP@

# حرکت برای زندگی بهتر

مصوب وزارت بهداشت، درمان و آموزش پزشکی کتابچه معرفی و شرح فعالیتهای سال ۱۳۹۸

## ییام ریاست مرکز

#### بنام خدا

#### «مرا اختر خفته بیدار گشت به مغز اندر اندیشه بسیار گشت»

بیست سال پیش در حالیکه علم پزشکی در آستانه انقلاب ژنتیک قرار داشت و اطلاعات مربوط به شبیه سازی در صدر اخبار بود، با گروهی از دانشجویان علوم پزشکی و علوم پایه فعالیتی پایه نهاده شد. ده سال بعد صدر اخبار را علوم و فنآوری های چهارگانه (NBIC) اشغال کرده بود و همکاران و موسسین مرکز، در کنار کار بالینی هنوز دلبسته دانش بودند و مشغول آموختن و آموزگاری.

همان روزها ایده تاسیس مرکزی با چشم اندازی یگانه در خدمت به بیماران، محلی برای گرامیداشت دانش و معرفت و انجمنی از دانش پیشگان در ذهن بود و تا امروز همچنان هرچند با گامهای کوتاه اما با استواری در این راه آمده ایم تا میراث بزرگ علم و دانش در ایران را گرامی بداریم و در افزایش سرمایه دانش و زایش دانشمندان جوان سهمی داشته باشیم.

ناگزیر در فرآیند توسعه پژوهش در ایران عزیز، ایده تاسیس مراکز خصوصی مطرح شد و چون معتقد بودیم و هستیم که فرآیند پژوهش و تولید فنآوری باید چابک و هدفمند باشد، با دقت نظر این مدل از همکاری علمی را برگزیدیم.

جمعی از پزشکان متخصص و فوق تخصص در جراحی های اعصاب، بیماری های عصبی، روانپزشکی و توانبخشی در کنار دانش پیشگانی از رشته های گوناگون علوم پایه و مهندسی با پیشنهاد تاسیس اولین مرکز خصوصی در این حوزه گرد هم آمدند. اندک اندک یاران جانی در بخشهای مدیریتی مرکز به ما اضافه شدند. بسیار با هم نشستیم و برخاستیم تا غبار منیت نشست و حجاب زبان از میان برخاست و همزبانی جای خود را به همدلی داد.

آنچه در پیش چشمان نکته سنج شما است انعکاس تصویر بخشی از تلاشهای همکاران مرکز تحقیقات مدولاسیون عصبی و درد است که با سرمایه گران بهای عمر عزیزان همکار و منابع مالی بخش خصوصی در آیینه صفحات منعکس شده، بسیارند تلاشهای مجدانه و مجاهدانه که با عسرت فراوان در حال انجام است و هنوز زمان پسرشان فرا نرسیده و میوه های بسیاری که امید باغبان بر نهال های تازه کاشته اش در ذهن دارد.

ایکاش دفتر حاضر مجالی برای نمایش کاهش آلام بیماران و شادی ناشی از بهبودی و بهروزی ایشان داشت، تا نتیجه واقعی و هدف اصلی مرکز را شما هم به تماشا و قضاوت می نشستید. همه تلاش ها برای این منظور بوده و خواهد بود و دستاوردهای دیگر فرعند بر این اصل.

کثرت همکاری با دانشمندان رشته های مختلف در وحدت ما و وحدت ما در خدمت به کثرت بیماران را شکرگزارم. قدمهای راسخ و استوار همه دانشمندان و دانش پیشگانی که با مرکز احساس یگانگی دارند در راه کاهش آلام بیماران و شکافتن سقف فلک از معرفت جدید، بر چشمان این کمترین.

حضور دانشجویان جوانی که با مرکز ما همکاری می کنند، شیرین ترین تصویر و برآورده شدن اولین و بزرگترین رویای موسسین است. بر همت این جوانان عاشق که پای در راه عشق به علم نهادند باید آفرین ها گفت و مرکز متعهد خواهد بود که بیشترین توان خود را مصروف همگنان بیست سال پیش موسسین امروز بگذارد.

«بی علم تو نتوانی کز پیه کشی روغن بنگر تو در آن علمی کز پیه نظر سازد»

دکتر علی رزم کن دکتر علیرضا مهدی زاده

## درباره ما

عمل جراحی تحریک عمقی مغز DBS بر روی بیمار مبتلا به پارکینسون برای نخستین بار در سال ۱۳۹۳ در شیراز، قطب پزشکی جنوب ایران، انجام شد. سایر اعمال جراحی تهاجمی و کم تهاجمی مدولاسیون عصبی شامل تحریک طناب نخاعی SCS در درمان درد، تحریک عصب خاجی SNM در درمان بی اختیاری، تحریک عصب واگ VNS در درمان تشنج، و کارگذاری یمیهای کاشتنی نخاعی بلافاصله در سالهای بعد، و مهمتر از همه تحریک عمقی مغز در درمان وسواس حبری توسط همین تیم جراحی انجام پذیرفت. انجام بیش از صد مورد از عمل های جراحی استریوتاکسی بر روی بيماراني با مشكلات مختلف اعم از ياركينسون، ديستوني، انواع مختلف لرزش و همچنين وسواس ما را بر آن داشت که با بهره گیری از تیمی مجرب، به انجام پژوهش در جنبه های مختلف اعمال جراحی فانکشنال و مدولاسیون عصبی بیردازیم و بررسی ایده های مفید در جهت افزایش بهبودی بیماران پس از عمـل را نیـز از اولویـت هـای کاری خـود بدانیـم. در ایـن راسـتا، ایـده ی تاسـیس یـک مرکـز تحقیقاتی خصوصی که به صورت خاص به پژوهشهای مرتبط در این خصوص بیردازد، در ذهن تيـم درمانـي مـا ايجـاد شـد. مركـز تحقيقـات مدولاسـيون عصبـي و درد، فعاليـت رسـمي خـود را از پاييـز سال ۱۳۹۷ آغاز نمود. این مرکز با داشتن حمایت اعضای متخصص در زیرشاخه های متنوع پزشکی، پیرایزشکی و مهندسی سعی بـر آن دارد کـه بـا اعتـماد بـه محققیـن و پژوهشـگران بتوانـد گامـی موثـر در افزایـش سـطح علمـی کشـور در زمینـه مدولاسـیون عصبـی و درد، بـردارد و خدمـات درمانـی شایسـته ای را در استاندارد بین المللی اما منطبق بر معیارهای بومی ارائه دهید.

## درباره مدولاسيون عصبى

مفهوم کلمه مدولاسیون در زبان فارسی، «ایجاد تغییرات در جهت بهبود» است و مدولاسیون عصبی یا نورومدولاسیون هم متعاقبا به معنای ایجاد تغییرات در سیستم عصبی به منظور بهبود شرایط خواهد بود.

پیشه ی نورومدولاسیون را باید در قرن های قبل از میلاد مسیح جستجو کرد؛ جایی که مصریان باستان از ماهی های رود نیل (ماهی تورپدو) که قادر به ایجاد حدود ۲۰۰ ولت الکتریسیته بودند برای کم کردن علائم افراد مبتلا به صرع استفاده می کردند.

رومیان باستان از این روش حتی در درمان نقرس نیز استفاده میکردند و جالب تر آنکه برخی قبایل بومی آفریقایی هنوز هم این یروسه را دنبال می کنند.

شاید بتوان اولین استفاده درمانی از تحریکات الکتریکی (که با داشتن علم نسبی در این زمینه همراه بوده) را به کریستین کراتزین اشتاین نسبت داد که در قرن ۱۸ میلادی آزمایشاتی را انجام داده است. در ادامه ی راه، فریتش و هیتزیش در قرن ۱۹ دریافتند که تحریک کورتکس مغزی منجر به انقباض عضلات می شود، و سال بعد از این آزمایش، بارتلو این آزمایش را بر روی انسان انجام داد و به نتایج مشابهی دست یافت.

آزمایشات این چنینی بسیاری در طول قرن های اخیر باعث تکامل و پیشرفت فیزیولوژی، نوروساینس، علوم مهندسی و همینطور تکنیک های جراحی؛ در شکل گیری نورومدولاسیون در قالب امروزی بسیار موثر بوده اند.

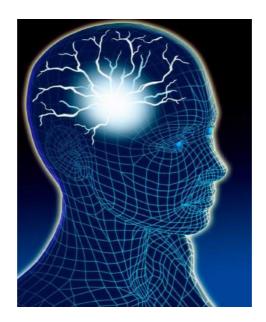
شاید در نگاه اول حیطه ی مدولاسیون عصبی حیطه ای پر زرق و برق با مخارج و هزینه های بالا به نظر بیاید اما بشر با علم به اثرات درمانی و کاهش کلی هزینه ها سعی در گسترش و کاهش کلردی تر کردن این زمینه ی درمانی داشته است.

پیشرفت ها و جایگاه امروزی مدولاسیون عصبی بدون سال ها تلاش، تحقیق و مخارج سنگین حاصل نشده است و فراوانی مقالات، کتب و کنفرانس هایی که سالانه در این باره در سراسر جهان برگزار می شوند موید این موضوع است.

به طور مثال در سال ۲۰۱۰ چیزی حدود ۳ تا ۴/۵ میلیارد دلار در سطح جهان صرف هزینه ی تحقیق،

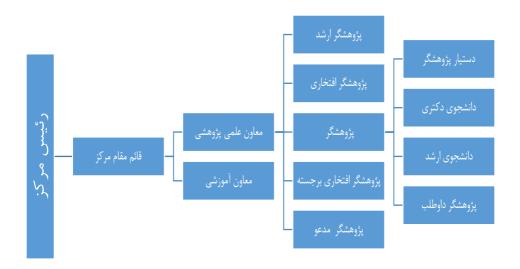


توسعه و مصارف درمانی نورومدولاسیون شده است که در نگاه اول مبلغ گزافی به نظر میرسد که حتی شاید منجر به نتایج مطلوبی نشده باشد؛ اما اگر بدانیم که طبق برآورد ها در همان سال، نتیجه ی یکسان در درمان بیماران نیازمند، از طریق دارو درمانی و نه مدولاسیون عصبی مبلغی حدود ۲۰ میلیارد دلار مخارج به دنبال داشت نظر و ذهنیت خود را از این حیطه تغییر می دهیم.



# چارت تشكيلاتي مركز تحقيقات

ساختار مدیریتی مرکز در نه ودار زیر به روشنی تشریح شده است. بخش اعظم نیروهای مرکز را نیروهای پژوهشی تشکیل می دهند.



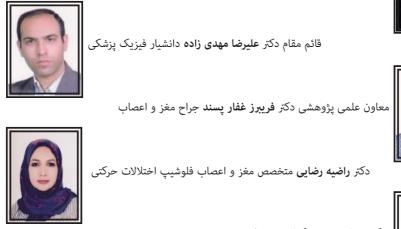
## اعضای مرکز

رئیس مرکز دکتر علی رزم کُن جراح مغز و اعصاب، فلوشیپ فانکشنال

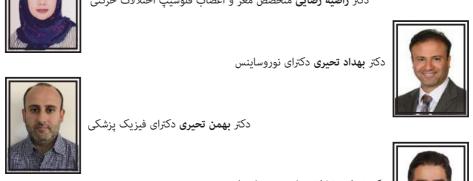






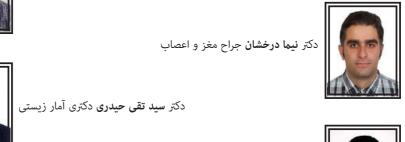










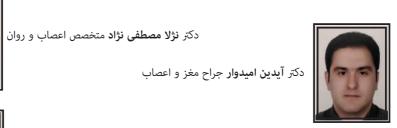


دکتر **سید پوریا استاد** متخصص رادیولوژی



## اعضاي مركز







دکتر غلامرضا ودیعی دستیار تخصصی جراحی مغز و اعصاب
دکتر امید یوسفی پزشک عمومی





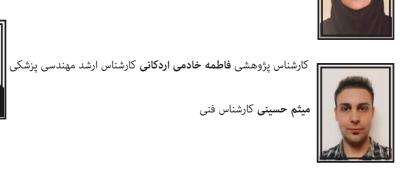




محمد حسین محمدی کارشناس ارشد مکانیک محمد محمدی کارشناس ارشد مکانیک مدیر مرکز سحر مشکسار دانشجوی دکترای مدیریت کسب و کار







## موافقت اصولى مركز تحقيقات

اخـذ موافقـت اصولـی مرکـز تحقیقـات خصوصـی مدولاسـیون عصبـی از وزارت محـترم بهداشـت در سال ۱۳۹۸



## نظر چهره های مشهور مدولاسیون عصبی دنیا در خصوص مرکز

پروفسور Joachim Krauss رئیس سابق جامعه جهانی جراحی اعصاب فانکشنال و استریوتاکتیک بابت راه اندازی جراحی اختلالات حرکتی در جنوب ایران به شما تبریک می گویم. موفقیت بسیار بزرگی است.





پرفسور Hans Speelman استاد سابق نورولوژی آمستردام تبریک به نتایج DBS در شیراز، اثبات کیفیت و استقامت تیم! Congratulations for the results of DBS in Shiraz: A proof of the quality and endurance of the team.

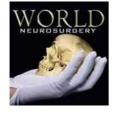
پروفسور Ludvic Zrinzo موسسه نورولوژی UCL Queen Square لندن

این واقعایک دستاورد فوق العاده است. نتایج شگفت انگیز عمل جراحی و مهمتر از آن، سخت کوشی مثال زدنی تیم شما برای اطمینان هرچه بیشتر از در دسترس بودن این روش برای شهروندان ایرانی.



HUGE congratulations! This is indeed a fantastic achievement. Wonderful results and, more importantly, amazing tenacity to ensure the procedure is available to as many Iranian citizens as possible.

مجله World Neurosurgery



این گروه موفق به راه اندازی یک مرکز درجه یک صرفا در کمتر از چند سال شده است.

I commend the authors for their hard work establishing this DBS program and taking the time and energy to do research in this regard. They have established a center offering top notch care within just a few years.

۱- مرکز تحقیقات پیر دونیکه، بیمارستان دانشگاهی هانری لابوری در پواتیه، فرانسه



Unite de recherche clinique Pierre Deniker, Centre Hospitalier Henri Laborit, CENTRE HOSPITALIER Henri Laborit Poitiers







۳- دبیر خانه ثبت بیماریها و پیامدهای سلامت دانشگاه علوم پزشکی ارومیه



٤- مرکز تحقیقات روانپزشکی و علوم رفتاری دانشگاه علوم پزشکی شیراز

#### محورهای اصلی فعالیت مرکز تحقیقات مدولاسیون عصبی و درد

#### ۱- خدمات درمانی

اعـمال جراحـی فـوق پیشرفتـه مدولاسـیون عصبـی ( اختـلالات حرکتـی، وسـواس جـبری، تشـنج، درد و بـی اختیـاری ادرار)

#### ۲- آموزش تخصصی

ایجاد فرصت جهت متخصصین مغز و اعصاب و جراحان مغز و اعصاب جهت یادگیری در زمینه مدولاسیون عصبی

#### ٣- آموزش پژوهش

آموزش اصول پژوهش به پژوهشگران جوان در جهت اهداف مرکز

## ٤- آموزش عمومي

آموزش به جامعه در جهت افزایش آگاهی و پیشگیری از بیماری های عصبی

#### ٥- يژوهش هاى بالينى

طراحی، مدیریت و انجام پژوهش های بالینی جهت پایش و بهبود کیفیت درمان

## ٦- پژوهش های بنیادی

طراحی، مدیریت و انجام پـروژه هـای بنیــادی و مهندســی در جهــت بومــی ســازی تکنولــوژی مدولاســیون عصبــی

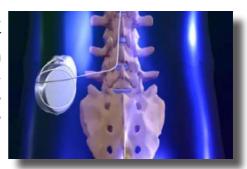


## خدمات درماني



## عمل جراحی تحریک عمقی مغز

درمان بیماری های پارکینسون، دیس تونی، لرزش و برخى اختلالات روانپزشكى همچون اختلال وسواس جبری توسط این تکنیک جراحی امکان پذیر می باشد. شیراز یک مرکز منحصر بفرد انجام این عمل جراحی در منطقه می باشد.



### عمل جراحی کارگذاری محرک نخاعی

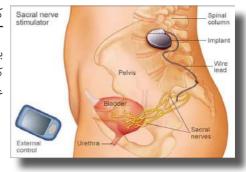
این عمل جراحی جهت بیمارانی که قبلا تحت عمل جراحی ستون فقرات قرار گرفته اند و مبتلا به درد شـدید سوزشـی در اندامها مـی باشـند، و یـا بیـماران دیابتی با چنین دردی مفید می باشد.



## کارگذاری پمپ های نخاعی

بیاران مبتلا به درد شدید اندامهای بدن، خصوصا به دنبال بدخیمی یا آسیبهای نخاعی، کاندید مناسبی برای کارگذاری این تکنولوژی پیشرفته هستند.

## خدمات درماني



## کارگذاری محرک عصب خاجی

بیمارانی که به علی متعدد دچار اختالال نسبی کنترل ادرار و مدفوع می باشند، می توانند تحت عمل جراحی کارگذاری این دستگاه قرار گیرند.

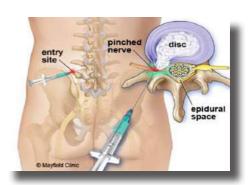


## اعمال جراحی جهت صرع

برخی از بیمارانی که علیرغم مصرف داروهای تشنج، بهبود کامل نیافته اند، می توانند طی پیشرفته ترین اعمال جراحی مغز و اعصاب، به صورت نسبی یا کامل بهبود یابند.

## درمان های کم تهاجمی درد

بیمارانی که دچار درد شدید صورت، کمر و یا گردن می باشند و به درمانهای محافظه کارانه پاسخ ندهند، می توانند از پیشرفته ترین درمانهای کم تهاجمی درد بهره جویند.



## آموزش تخصصی و آموزش پژوهش

مركز مدولاسيون عصبى و درد از ابتداى تاسيس تا كنون، آموزش تحقيق و همچنين تعليم افراد علاقه مند در حیطه ی مدولاسیون عصبی را جز اهداف خود دانسته و از این رو تا کنون با برگزاری کنفرانس های علمی، سعی در تعلیم پژوهشگران علاقمند داشته است.

در هر یک از جلسات این کنفرانس های علمی یکی از ابعاد نورومدولاسیون ارائه شدند و علاقمندان به این حیطه در این کنفرانس ها شرکت کرده اند. مباحث مطرح شده در این کنفرانس ها، تا کنون زمینه های مطرح شدن و ادامه یافتن بسیاری از طرح های پژوهشی مرکز شده اند.

## اولىن جلسه

موضوع Gait Analysis

ارائه دهنده : دکتر بهداد تحبری

ىه تارىخ ۹۷/۰۹/۰۳

در این جلسه دکتر تحیری، دکترای نوروساینس، پیرامون مشکلات راه رفتن در بیماران پارکینسونی و نحوه ی بررسی و بهبود شرایط بیماران به توضیح پرداختند.



## 1st Scientific Lecture of Center for Neuromodulation and Pain



Title: Gait Analysis Presented by: Dr.Behdad Tahayori Date: 97/09/03 Location: Fourth Floor, Zand Building, Zand St, Shiraz



دومین جلسه

موضوع Brain Computer Interference

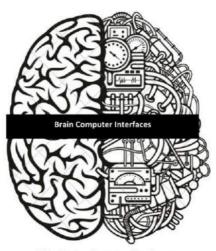
ارائه دهنده : دكتر فريبرز غفار يسند

به تاریخ ۹۷/۰۹/۱۷

در این جلسه دکتر فریبرز غفار پسند، جراح مغز و اعصاب، به موضوع جذاب راه های ارتباطی مغز و کامپیوتر پرداختند.



## 2<sup>nd</sup> Scientific Lecture of Center for Neuromodulation and Pain



Title: Brain- Computer Interference Presented by: Dr.Fariborz Ghaffarpasand

Date: 97/09/17



#### سومين جلسه

موضوع Electromagnetic Field Effects on Neuromodulation and Pain

ارائه دهنده : دکتر علیرضا مهدی زاده

به تاریخ ۹۷/۱۰/۰۵

در این جلسه دکتر علیرضا مهدی زاده، دکترای فیزیک پزشکی، در مورد کاربرد الکترومغناطیس در حیطه ی نورومدولاسیون پرداختند.



# 3rd Scientific Lecture of Center for Neuromodulation and Pain



Title: Electromagnetic Field Effects on Neuromodulation and Pain Control

Presented by: Dr. Alireza Mehdizadeh

Date: 97/10/05



چهارمىن جلسه

موضوع An Introduction to Neuroprosthetics with Focus on the Bionic Eye

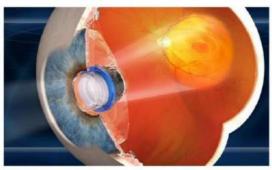
ارائه دهنده : دکتر بهمن تحیری

به تاریخ ۹۷/۱۰/۲۲

در این جلسه دکتر بهممن تحیری، دکترای فیزیک پزشکی، در مورد آخرین تحقیقات در مورد چشم بیونیک توضیح دادند.



# 4th Scientific Lecture of Center for Neuromodulation and Pain



Title: An Introduction to Neuroprosthetics with Focus on the Bionic Eye

Presented by: Dr.Bahman Tahayori

Date: 97/10/22 Time: 1-3pm



ينجمين جلسه

موضوع Psychiatric Disorders in Parkinson's Disease

ارائه دهنده : دكتر نژلا مصطفى نژاد

به تاریخ ۹۷/۱۱/۱۰

در این جلسه دکتر نژلا مصطفی نژاد، متخصص روانپزشکی، به توضیح در مورد مشکلات شایع روانیزشکی در میان بیماران مبتلا به پارکینسون پرداختند.



# 5th Scientific Lecture of Center for Neuromodulation and Pain



Title: Psychiatric Disorders in Parkinson's Patients

Presented by: Dr.Mostafanejad Date: 97/11/10

Time: 1-3pm



#### ششمين جلسه

موضوع Neuroelectric Biomarkers of Network Dysfunction in AML

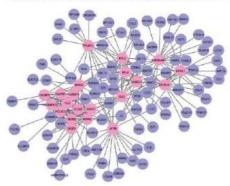
ارائه دهنده: دكتر بهمن ناصر الاسلامي

به تاریخ ۹۷/۱۲/۰۴

در این جلسه دکتر ناصرالاسلامی، دکترای فیزیک پزشکی، در یک تله کنفرانس از دوبلین، به تغییرات شبکه های عصبی در بیماری MS پرداختند.



## 6th Scientific Lecture of Center for Neuromodulation and Pain



Title: Neuroelectric Biomarkers of Network Dysfunction in **Amyotrophic Lateral Sclerosis** 

Presented by: Dr. Bahman Nasseroleslami

Senior Research Fellow and Principal Investigator Academic Unit of Neurology, Trinity College Dublin, the University of Dublin, Dublin, Ireland.

Date: 97/12/04

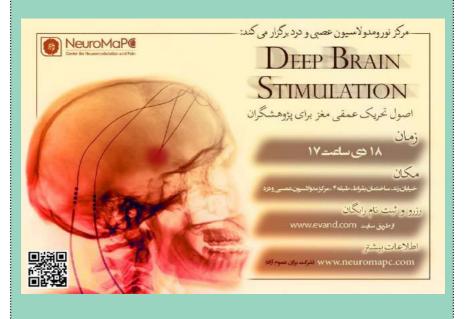
Time: 12:30-14:30

Location: Ordibehesht St. between Haftetir and Poostch i St., Peyvand Lab



## هفتمين جلسه موضوع Deep Brain Stimulation ارائه دهنده : دکتر امید یوسفی به تاریخ ۹۸/۱۰/۱۸

در این جلسه، دکتر امید یوسفی از پژوهشگران مرکز، در مورد عمل جراحی DBS در بیماران یارکینسونی توضیحاتی ارائه دادند.



## هشتمین جلسه موضوع Neuromodulation ارائه دهنده : دکتر علی رزم کُن به تاریخ ۹۸/۱۱/۲۸

در این جلسه دکتر رزم کُن، رییس مرکز، در مورد انواع حیطه های مدولاسیون عصبی و کاربرد های آنها توضیحاتی ارائه کردند.



# آموزش تخصصی و آموزش پژوهش

#### کارگاه:

یکی دیگر از اهداف مرکز مدولاسیون عصبی و درد، تعلیم نیروی متخصص برای ارائه ی بهتر درمان به بیماران نیازمند میباشد. از این رو جلسات آموزشی مرکز در جهت گسترش این هدف، در طی دو سال گذشته دایر بوده و برنامه ریزی ها جهت پیشبرد سریع تر این موضوع از اولویت های مرکز است.

جلسه ی آشنایی و آموزش تحریک عمقی مغز برای متخصصین نورولوژیست و جراحان مغز که در تاریخ اسه ی آشنایی و دکتر رضایی، جراح و ۱۳۹۸/۰۷/۱۲ به میزبانی آزمایشگاه پیوند برگزار شد. در این جلسه دکتر رزم کُن و دکتر رضایی، جراح و نورولوژیست تیم تحریک عمقی مغز، به توضیح در مورد مراحل جراحی بیماران پارکینسونی پرداختند و در ادامه، دکتر وایدیاناتان، سخنران بین المللی مدعو نیز به جزئیات تکمیلی اشاره کردند.



# آموزش تخصصی و آموزش پژوهش

## کارگاه:

در یکی دیگر از این جلسات آموزشی، برای پایش بهتر و همچنین کمک به بیماران پارکینسونی که افکار و یا تمایلاتی نسبت به خودکشی دارند، دکتر سارا پاشنگ پژوهشگر مهمان از دانشگاه پوآتیه فرانسه در مورد چگونگی استفاده از ابزارهای نوین سنجش تمایل به خودکشی در بیماران، به توضیح پرداختند.





کنفرانس یک روزه کاربردهای تحریک عصب واگ VNS در درمان صرع و افسردگی

کنفرانے سے کر روزہ کاربردھای تحریک عصب واگ VNS در درمان صرع و افسردگی با همکاری بخش نورولوژی، روانپزشکی و جراحی اعصاب دانشگاه علوم پزشکی شیراز، پنج شنبه پنجم دی ۹۸ در تالار اقبال لاهوری بیمارستان نمازی با حضور اساتید و متخصصان و جراحان مغز و اعصاب برگزار شد. در این سمینار، دكتر على رزم كُن جراح و متخصص مغز و اعصاب و رئيس مركز مدولاسيون عصبي و درد به ارايه سخنراني در باب تکنیک جراحی VNS پرداخت.



## جلسه دفاع نخستین پایان نامه تخصصی انجام شده در مرکز

جلسه دفاع از پایان نامه تخصص روانپزشکی سوم اسفندماه ۹۸ توسط خانم دکتر مصطفی نژاد که نخستین پایان نامه مشترک دانشگاه با مرکز تحقیقات مدولاسیون عصبی به شمار می آید. این پژوهش حاوی نتایج بسیار جذاب و مهمی شامل بهبود علایم افسردگی و اضطراب و تکانشی در بیماران پس از روشن شدن دستگاه می باشد. در این جلسه، پروفسور جعفری از بزرگترین روانپزشکان فرانسه و اروپا در زمینه جراحی اختلالات روانی از طرف مرکز نورومدولاسیون شیراز حضور داشتند. از راست به چپ: دکتر مانی، دکتر دستغیب، پروفسور جعفری، استاد جوادپور، خانم دکتر مصطفی نژاد، دکتر رزم کُن و دکتر مولا.

# آموزش تخصصی و آموزش پژوهش

## پایان نامه های انجام شده با حمایت مرکز



فريده مؤمني



دکتر امید یوسفی



دکتر نژلا مصطفی نژاد

## یایان نامه های در دست انجام



دكتر ليلا كلهر



محمد حسين محمدي



دكتر سمانه خضرايي

## جایزه محقق برتر جشنواره رازی





بیشترین تعداد داوری انجام شده توسط یک داور در یکی از مجلات Elsevier



جایزه بهترین پژوهش دانشجویی کنگره جراحان مغز آمریکا



# یایگاه داده آنلاین مرکز

مرکز تحقیقات مدولاسیون عصبی و درد در راستای انجام و هدایت پروژه های بزرگ پژوهشی در زمینه مدولاسیون عصبی اقدام به تاسیس دو پایگاه داده آنلاین و جامع نموده تا با اعطای دسترسی به پژوهشگران علاقهمند به حیطه نورو مدولاسیون، زمینه ساز اجرای پروژه های پژوهشی متعدد در این زمینه گردد.

#### ۱. پایگاه دادههای بیمارانی که تحت عمل DBS قرار گرفته اند:

شامل اطلاعات دموگرافیک، فیلم ها و پارامتر های تحریکی و تغییرات این پارامتر ها، قبل و بعد از عمل کلیه بیمارانی است که به دلیل پارکینسون، وسواس و دیستونی تحت عمل جراحی قرار گرفته اند. امکان آنالیز کوچک ترین موارد نیز بنا بر درخواست ممکن می باشد.

#### ۲. پایگاه داده بیماران پارکینسونی:

با توجه به این که جراحی پارکینسون انحصارا در در این مرکز انجام می گیرد، ماهانه ۲۰۰ بیلمار از سراسر کشور و حتی خارج از کشور به این مرکز مراجعه می کنند که تمامی بیلماران به محض ورود توسط نورولوژیست و روانپزشک، روانشناس و سایر متخصصین مرتبط ویزیت می شوند و فرم های اختصاصی بیلماران تکمیل می شود و اطلاعات آن ها با رضایت آگاهانه بیلماران در این پایگاه داده ثبت می گردد که منبع بسیار خوبی برای پژوهشگران است. آنلاین بودن این پایگاه های داده این امکان را به پژوهشگران خواهد داد تا بتوانند در هر کجای کره خاکی که هستند از این اطلاعات استفاده نمانند.

## یژوهش های بنیادی و کاربردی

#### الف: مطالعات تهاجمي مغز

مطالعات تهاجمی برای بیماری های حرکتی: با توجه به ناتوانی دارو درمانی در درمان مراحل پیشرفته بیماری های حرکتی همچون پارکینسون و دیستونی، این مرکز در راستای بهبود کیفیت زندگی این بیماران همواره در حال مطالعه بر روی DBS و پارامتر های آن و تاثیر این تغییرات بر روی مواردی همچون تاکنون و عوارض غیر موتور این بیماران میباشد. مطالعه ای در مورد کیس های عمل شده پارکینسونی تاکنون چاپ یا انجام میباشد.

مطالعات تهاجمی برای بیماری های روانپزشکی: این مرکز از پیشگامان Psychosurgery در منطقه بوده و ۴ مقاله از بیماران عمل شده و سایر موضوعات در این حیطه در حال چاپ و انجام میباشد.

#### ب: مطالعات غير تهاجمي مغز

مطالعات غیر تهاجمی برای بیماری های حرکتی و سایر ناتوانی های جسمی: به علت تهاجمی بودن DBS، هزینه زیاد این عمل ها، مناسب نبودن بعضی از بیماران برای تحریک عمقی مغز و همچنین مطالعات جدید بر روی روش های غیر تهاجمی تحریک مغز این مرکز نیز بر روی این دسته از مداخلات در حال مطالعه است. بررسی تحریکات سطحی در بیماران ترومای مغزی و پارکینسونی از جمله ای تحقیقات است. ۲ مطالعه در مرکز در حال انجام است.

مطالعات غیر تهاجمی برای بیماری های روانپزشکی: بنابر دلایل گفته شده برای مطالعه بر روی مداخلات غیر تهاجمی مغز بر روی بیماران حرکتی، مطالعاتی نیز بر روی بیماران بیماری های روانپزشکی به صورت تحریکات سطحی در حال انجام است.

## ج: مطالعات مربوط به حیطه تصویر برداری

با توجه به نیاز روز افزون مرکز برای بهبود کیفیت و تصویر برداری بهتر برای استفاده در مداخلات تهاجمی، مرکز در حال مطالعه روش های جدید تصویر برداری و اسکن هسته ای در بیماران به کمک گروه های فیزیک پزشکی، پزشکی هسته ای و رادیو لوژی است. در این دسته نیز ۴ مطالعه در حال انجام میباشد.

## گروه دانشجویی مرکز تحقیقات

## هماهنگ کننده: سعید عبداللهی فرد



زهرا شريفي



اميرحسين سعيدى



هيراد رضاعي



امیر بهادری



مبينا اميرسليماني



مرضیه کرمی راد



حسن فروزند



عرفان طاهري



كيوان صاحبي



كامياب شهريور



هومان كامران



عليرضا هنر





علی سینا میرزایی

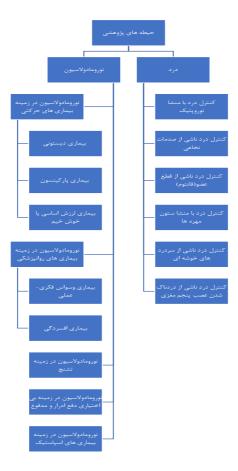


حميدرضا محقق

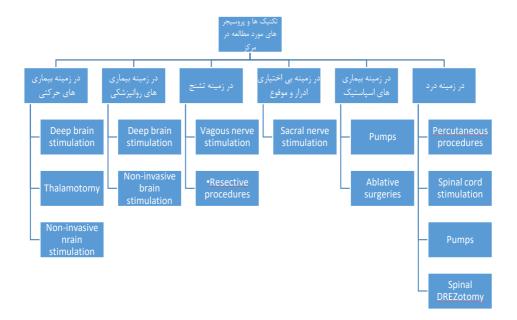
## دانشجو و پژوهشگر گرامی

این مرکز تحقیقاتی نه تنها به انجام پروژه های بین المللی، داخلی و همکاری با پژوهشگرانی که سابقه قبلی پژوهش دارند پرداخته، بلکه به آموزش افراد علاقه مندی که تجربه ای در این زمینه ندارند نیز می پردازد. همکاری با افراد علاقه مند صرفا در بحث پژوهشی نبوده و افراد داوطلب میتوانند در زمینه های فرهنگی، شبکه های اجتماعی و مدیا نیز به فعالیت بپردازند. ما به تمامی افراد علاقه مند خوش آمد می گوییم.

با توجه به نیاز وجود رویه ای منظم برای جذب دانشجویان و همچنین مشخص بودن نحوه همکاری با دانشجویان، بر آن شدیم تا به توضیح این الگوریتم در مرکز بپردازیم. پیش از اینکه به توضیح این رویه بپردازیم، حیطه های پژوهشی این مرکز را مرور میکنیم.



این مرکز مفتخر است که بیش از ده نوع پروسیجر مختلف را در زمینه های درد و نورومدولاسیون به انجام می رساند. شرح دقیق این مداخلات در فلوچارت زیر قابل ملاحظه است.



### نحوه همکاری با پژوهشگران و علاقه مندان

افراد داوطلب مى توانند از طريق آدرس ايميل زير:

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در صورت هرگونه سوال در مورد روند فوق و یا نحوه همکاری غیرپژوهشی با مرکز، داوطلبان میتوانند با ایمیل فوق در ارتباط باشند.

### آموزش عمومى

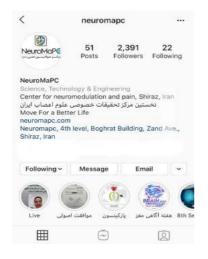
یکی دیگر از اهداف ۲ گانه ی این مرکز، آموزش برای عموم جامعه میباشد. بالا بردن اطلاعات جامعه در مورد بیماری های مختلف از جمله پارکینسون، به تشخیص بهتر و سریع تر بیماری و کمک به افراد مبتلا، کمک شایانی میکند.

از این رو مرکز مدولاسیون عصبی و درد در طی دو سال گذشته، همزمان با ماه و روز جهانی آگاهی از پارکینسون، وظیفه ی خود دانسته که در جهت افزایش آکاهی مردم کشور در مورد بیماری پارکینسون تلاش کند.

در فروردین سال ۱۳۹۸ جلسه ای به میزبانی بیمارستان کوثر شیراز، با حضور فرهیختگان علمی و همچنین تعدادی از مبتلایان به بیماری پارکینسون و خانواده های این عزیزان برگزار شد. اما در سال ۱۳۹۹، با توجه به پاندمی ویروس کرونا، تصمیم بر استفاده از ظرفیت شبکه های مجازی گرفته شد و در طی هفته ی آگاهی از بیماری پارکینسون، روزانه مطالبی علمی به اشتراک گذاشته می شد.











در کنار تلاش مستمر در آموزش تخصصی به پژوهشگران، متخصصین و دانشجویان رشتههای مرتبط، تلاش در جهت ارتقاء دانش عمومی جامعه در خصوص بیماریهای هدف مدولاسیون عصبی از جمله اختلالات حرکتی و روانی، از مهمترین اهداف مرکز تحقیقات مدولاسیون عصبی و درد میباشد. در این راستا و علاوه بر برگزاری همایش سالیانه روز جهانی پارکینسون با حضور پزشکان و بیماران، تارفای مرکز تحقیقات به آدرس neuromapc.com و حساب اینستاگرام neuromapc حاوی اطلاعات چندرسانهای آموزشی جذاب به زبان ساده در خصوص موارد ذکر شده میباشد.

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Rescue Thalamotomy in a Case of Holmes Tremor: A Case Report and Review of the Literature	Yousefi, Janardan Vaidyanathan	and Functional Neurosurgery	PubMed, Embase	1.47
Initial Results of Bilateral Subthalamic Nucleus Stimulation for Parkinson Disease in a Newly Established Center in a Developing Country: Shiraz, Southern Iran	Ali Razmkon, Omid Yousefi, , Janardan .Vaidyanathan, et al	World neurosurgery	ISI, Scopus, PubMed, Embase	1.570
Neurotrauma as an Evolving Indication for Neuromodulation	Ali Razmkon	Bulletin of Emergency & Trauma	PubMed, Embase	2.139
Exercise induced operant conditioning of the H-reflex in stroke patients: Hopes for improving motor function through inducing plastic changes in the spinal pathways.	Behdad Tahayori* and David Koceja	Journal of Neurology, Neurological Science and Disorders	ISI, Scopus, PubMed,	
Effects of cerebrolysin on functional outcome of patients with traumatic brain injury: a systematic review and meta-analysis	Fariborz Ghaffarpasand, et al.	Neuropsychiatric Disease and Treatment Vols. 1 to 16; 2005 to 2020	ISI, Scopus, PubMed, Embase, DOAJ	2.157
Intravenous Acetaminophen (Paracetamol) for Postcraniotomy Pain: Systematic Review and Meta-Analysis of Randomized Controlled Trials	Fariborz Ghaffarpasand, et al.	World neurosurgery	ISI, Scopus, PubMed, Embase	1.570
Determinants of reoperation after decompressive craniectomy in patients with traumatic brain injury: A comparative study	Fariborz Ghaffarpasand, et al.	Clinical neurology and neurosurgery	ISI, Scopus, PubMed, Embase	0.46
Tranexamic Acid; A Glittering Player in the Field of Trauma	Fariborz Ghaffarpasand, et al.	Bulletin of Emergency & Trauma	PubMed, Embase	2.139
Risk Factors of Neural Tube Defects in a Sample of Iranian Population from Southern Iran; a Hospital-Based Investigation	Fariborz Ghaffarpasand, et al.	The Iranian Journal of Neurosurgery (Iran. J. Neurosurg)	DOAJ	



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Ventrolateral Preoptic Nucleus of Hypothalamus; A Possible Target for Deep Brain Stimulation for Treatment of Sexual Dysfunction	Fariborz Ghaffarpasand, et al.	The Iranian Journal of Neurosurgery (Iran. J. Neurosurg)	DOAJ	
MicroRNA-199a Upregulation Mediates Lumbar Interverte- Fariborz Ghaffarpasand, bral Disc Degeneration and is Associated with Clinical et al.	Fariborz Ghaffarpasand, et al.	Turkish neurosurgery (TURK NEUROSURG)	ISI, Scopus, PubMed	0.25
Determination of miRNA-199a and its Target Genes in Degenerative Lumbar Intervertebral Disc	Fariborz Ghaffarpasand, et al.	Turkish neurosurgery (TURK NEUROSURG)	ISI, Scopus, PubMed	0.25
Clinical outcome of V-Y flap with latissimus dorsi and gluteal advancement for treatment of large thoracolumbar myelomeningocele defects: a comparative study	Fariborz Ghaffarpasand, et al.	Journal of neurosurgery	ISI, Scopus, PubMed, Embase	3.630
In Reply to "Noncoding Ribonucleic Acid Studies of Lumbar Disk Disease: Decade Retrospect"	Fariborz Ghaffarpasand, et al.	World neurosurgery	ISI, Scopus, PubMed, Embase	1.570
MicroRNA Expression Profiles, Target Genes, and Pathways Fariborz Ghaffarpasand, in Intervertebral Disk Degeneration: A Meta-Analysis of 3 det al. Microarray Studies	Fariborz Ghaffarpasand, et al.	World neurosurgery	ISI, Scopus, PubMed, Embase	1.570
Review of Renal Biopsies, A Single Center Experience	Omid Yousefi, et al.	Iranian Journal of Kidney Diseases		1.150
Determinants of reoperation after decompressive craniecto- my in patients with traumatic brain injury: A comparative et al.	Fariborz Ghaffarpasand, et al.	Clinical neurology and neurosurgery	ISI, Scopus, PubMed, Embase	0.46



### **Case Report**

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### Using Preimplanted Deep Brain Stimulation Electrodes for Rescue Thalamotomy in a Case of Holmes Tremor: A Case Report and Review of the Literature

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### Keywords

 $Holmes\ tremor \cdot Rescue\ thalamotomy \cdot Lesioning \cdot Deep \\brain\ stimulation$ 

### Abstract

Background: Chronic stimulation of the thalamus is a surgical option in the management of intractable Holmes tremor. Patients with deep brain stimulation (DBS) can encounter infection as a postoperative complication, necessitating explantation of the hardware. Some studies have reported on the technique and the resulting efficacy of therapeutic lesioning through implanted DBS leads before their explantation. Case Description: We report the case of a patient with Holmes tremor who had stable control of symptoms with DBS of the nucleus ventralis intermedius of the thalamus (VIM) but developed localized infection over the extension at the neck, followed by gradual loss of a therapeutic effect as the neurostimulator reached the end of its service life. Three courses of systemic antibiotic therapy failed to control the infection. After careful consideration, we decided to make a rescue lesion through the implanted lead in the right VIM before explanting the complete DBS hardware. The tremor was well controlled after the rescue lesion procedure, and the effect was sustained during a 2-year follow-up period. Conclusion: This case and the previously discussed

ones from the literature demonstrate that making a rescue lesion through the DBS lead can be the last plausible option in cases where the DBS system has to be explanted because of an infection and reimplantation is a remote possibility.

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### Introduction

Holmes tremor (HT) occurs after a lesion involving the cerebellum, midbrain, or thalamus [1, 2]. Such lesions are usually a result of hemorrhage, trauma, tumors, or infection [3–10]. Lesions affecting specific tracts, such as the cerebellothalamic or nigrostriatal tract, are considered the main cause of HT [2, 11–13]. It is a combination of resting, postural, and intention tremor.

In some cases, the tremor is responsive to different medical treatments. However, for the majority of patients, medication fails to alleviate the tremor, in which case stereotactic interventions are considered [14–16]. Studies have shown the efficacy of ablative and stimulation procedures in the management of HT. Sometimes, thalamotomy may have some short- and long-term complications, which may not be reversible and manageable [8, 17]. Deep brain stimulation (DBS) of the nucleus ventralis intermedius of the thalamus (VIM) could be care-

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Initial Results of Bilateral Subthalamic Nucleus Stimulation for Parkinson Disease in a Newly Established Center in a Developing Country: Shiraz, Southern Iran

Ali Razmkon<sup>1</sup>, Omid Yousefi<sup>1</sup>, Raziyeh Rezaei<sup>1</sup>, Sina Salehi<sup>2</sup>, Peyman Petramfar<sup>2</sup>, Arash Mani<sup>1</sup>, Hashem Rahmati<sup>2</sup>, Janardan Vaidyanathan<sup>6</sup>, Ghazal Ilami<sup>1</sup>, Yalda Amirmoezzi

# OBJECTIVE: To report the establishment of a new center for deep brain stimulation (DBS) as a surgical treatment for Parkinson disease and the surgical outcomes, from 2014 to 2017 in Shiraz, Southern Iran.

# METHODS: A new treatment program was established in Shiraz through a multidisciplinary team in 2014. Thirty-four patients underwent implantation of subthalamic nucleus (STN) electrodes during the last 3 years. Twenty-five patients fulfilled the minimum 6-month follow-up criteria. The baseline Unified Parkinson Disease Rating Scale (UPDRS) was assessed 1 month before surgery in both offmedication and on-medication states by a movement disorder neurologist. To evaluate the outcomes, subscores of the UPDRS were assessed in all patients before surgery and at least 5 months after the operation.

RESULTS: All 25 patients had advanced Parkinson disease categorized as stage 3 or 4 using the Hoehn and Yahr scale. STN DBS resulted in a dramatic improvement in motor function of most patients. A reduction in dopaminergic medication dosage (average 60% reduction) was observed. The mean improvement was 40% in UPDRS II and 67% in UPDRS III. No surgical or hardware complications were observed. Stimulation-related adverse effects, including increased falling and worsening of speech, occurred in a few patients after surgery. Most of the patients experienced weight gain after surgery.

CONCLUSIONS: Bilateral STN DBS is a satisfactory and safe treatment for carefully selected patients with advanced Parkinson disease. According to the results, the procedure can be performed salely and with comparable results in developing countries around the world,

#### INTRODUCTION

eep brain stimulation (DBS) is an effective therapy for Parkinson disease, tremor, dystonia, and other complex neurologic and psychiatric disorders. This therapy has been used since 1990 in many centers across the world.1 Although expensive and technically demanding, DBS is performed frequently, and numerous publications have documented its safety, benefits, and adverse events. 55 According to the current literature, the mean improvement in Unified Parkinson Disease Rating Scale (UPDRS) III is reported to be between 28% and 71% after surgery. 60 The surgery also results in 19-72% medication reduction among patients. toria Although DBS is expensive, strong pharmacoeconomic studies show that, in the long term, it reduces the cost of care in surgically treated patients.13

The population of Iran (approximately 80 million people) is aging rapidly. More than 6% of the population is older than 60 years, which is estimated to rise steeply to 10.5% by 2025.14 This fact increases the likelihood of acquiring neurodegenerative diseases, such as Parkinson disease, leading to increased disease burden and costs. Population-based, door-to-door studies have shown the prevalence of Parkinson disease to be as high as 285 per 100,000 population in Iran, which is considered a medium-to-high rate, 14,15 This prevalence necessitates the need to introduce new treatment modalities that will reduce disease burden. Shiraz is a major city in southwest Iran and is the referral medical center for the southern half of the country, covering at least 25 million

### Key words

Deep brain stimulation

Developing country

Farkwison disease

Subthalamic nucleus

Abbreviations and Acronyms DBS: Deep brain stimulation

INS: Implantable neurostimulator

MRI: Magnetic resonance imaging

STN: Subthalamic rucleus

UPDRS: Unified Parkinson Disease Rating Spale

From the <sup>4</sup> Reveach Center for Neuropadulation and Pain, Kowcar Hozoital, Shiraz <sup>2</sup> Shiraz Neuroscience Research Center. \*Department of Neurology, \*Research Center for Psychiatry and Behavioral Sciences, and <sup>6</sup>Community-based Psychologic Care Research Center, Shirar University of Medical Sciences, Shirar, Inst., and <sup>6</sup>Meditronic, Munical, India

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Editorial







### Neurotrauma as an Evolving Indication for Neuromodulation

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#### Keywords: Neurotrauma; Indication; Neuromodulation.

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Trauma is a major cause of morbidity and mortality in developing countries. With the advent of life-saving procedures and better inpatient care in trauma-specialized centers in our country, more and more patients are getting their lives back although with residual handicaps, disabilities and pain. Specific therapies must be used to increase quality of life and decrease pain and sufferings in trauma patients, when most of them are young and in their productive ages. Ablative neurosurgical procedures have been used in the past to treat different neurological diseases with significant irreversible side effects. They were useful in controlling pain or improving abnormal movements or behaviors in patients. Recently, many, albeit not all ablative surgeries have been replaced by neuro-stimulative technologies, which can produce the same effects but reversibly, so unwanted complications may be avoided

Neuromodulation refers to a specific subgroup of minimally invasive procedures aiming to provide therapeutic electrical stimulation to a predesigned field of the nervous system, so the whole system may work more efficiently to reduce pain and movement disorders, and to improve quality of life [1]. Among minimally-invasive procedures, different techniques exist, including deep brain, spinal cord, peripheral

nerve and sacral nerve stimulation procedures. Trauma patients have not been an ideal indication for most of these procedures; however, with the advent of newer generation of technologies, trauma is now trying to be re-considered as an evolving indication. Since 2014 we have started different techniques of neuromodulation in Shiraz for various indications. Due to the high rate of trauma patients in the region, traumatic brain and spinal cord injuries are being considered as common indications in our center.

### Deep Brain Stimulation (DBS)

DBS is commonly used in patients with movement disorders (mainly Parkinson's disease, dystonia and tremor) and psychiatric indications. Early reports from the positive effect of deep brain stimulation on patients suffering from severe traumatic brain injury [2] have been promising, and the first prospective study of DBS in these patients has proven its safety and potential effectiveness for functional independence in future [3]. More clinical research is necessary to bring DBS into clinical practice for trauma patients.

### Spinal Cord Stimulation (SCS)

Spinal cord or dorsal colmn stimulation has been used in a variety of different neurological conditions

Journal compilation © 2017 Trauma Research Center, Shiraz University of Medical Sciences

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### Journal of Neurology, Neurological Science and Disorders

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Keywords: Cerebrovascular accident (CVA): H-reflex; Operant conditioning: Inhibition

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#### Research Article

Exercise induced operant conditioning of the H-reflex in stroke patients: Hopes for improving motor function through inducing plastic changes in the spinal pathways

#### Abstract

Background: Cerebrovascular accident is a major cause of disability. Stroke survivors suffer from various severity levels of movement, impairment which would substantially affect their quality of life. Several methods have been investigated for improving movement in these patients. Most of the treatment approaches are geared toward inducing neuroplasticity in the brain. Here, we introduce a novel method to induce neuroplasticity in signal cord to compensate the overbort insult.

Purpose: The aim of this study was to examine the ability of hemiplegic stroke patients to volitionally down-regulate the soleus H-reflex and its functional consequence. A humancomputer interface was developed to monitor several neural and behavioral factors while subjects stood on a balance board. The interface would elicit an H-reflex when the criteria were met and would provide feedback to the patients about the amplitude of the H-reflex. Subjects were encouraged to down-regulate the amplitude of the reflex.

Results: The protocol was tested in 3 hemiplegic subjects. Subjects demonstrated the ability to describe the H-reflex. The rate of success in this down-regulation was on average %80.119.96. This success rate was in strong agreement with improvement in galt symmetry and gait velocity.

Major findings: This study demonstrated that stroke survivors have the ability to down-regulate their spinal reflexes and this down-regulation was correlated with movement improvement. Conclusion. The results suggest that stroke patients have the ability to down-regulate the Hreflex amid corticospinal damages. This was accompanied by improvement in motor function.

Potential implications: The current study has provided proof of evidence to show that inducing plate changes in the spinal cord can improve motor output in stroke survivors. This method could be another treatment approach for stroke impairment.

### Abbreviations

CVA: Cerebrovascular Accident; TA Tibialis Anterior; H-reflex: Hoffman Reflex; CPN: Common Peroneal Nerve; SL: Step Length; GII: Gait Improvement Index: SR: Success Rate

### Introduction

A cerebrovascular accident (CVA) is a leading cause of death and disability worldwide [1]. In recent years, several modern rehabilitation methods have been introduced and successfully tested [2-7]. The significance of these attempts is that they have utilized new technologies to bring basic concepts in neuroscience into clinical trials. This is especially critical for patients who are assumed to have been plateaued or do not show substantial improvement with other traditional therapy methods.

In line with the recent endeavors in stroke rehabilitation, we designed a novel method with the purpose of inducing plastic changes in lower motoneurons to compensate the function of upper motoneurons. The potential of spinal circuits as a site for neurorehabilitation are largely ignored in stroke rehabilitation. Here we used a well–established notion from

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Citation: Tahayori B, Koceja D (2019) Exercise induced operant conditioning of the H-reflex in stroke patients: Hopes for improving motor function through inducing plastic changes in the spinal pathways. J Neurol Neurol Sci Disord 5(1): 001-005. DOI: http://dx.doi.org/10.17352/jnnsd.0000026

### Neuropsychiatric Disease and Treatment

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ORIGINAL RESEARCH

# Effects of cerebrolysin on functional outcome of patients with traumatic brain injury: a systematic review and meta-analysis

This article was published in the following Dove Medical Press journal: Neuropsychiatak Disease and Treatment

Fariborz Ghaffarpasand<sup>1</sup> Saeed Torabi<sup>2</sup> Ali Rasti<sup>3</sup> Mohammad Hadi Niakan<sup>4</sup> Sara Aghabaklou<sup>3</sup> Fatemeh Pakzad<sup>6</sup> Maryam Sadat Beheshtian<sup>7</sup> Reza Tabrizi<sup>8</sup>

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Trauma Research Center, Rajaei Trauma Hospital, Shiraz University of Medical Sciences, 6th Floor, Chamran Avenue, Shiraz 4818684668, Iran Tel +98 921 670 7983 Email hadiniakan@yahoo.com Background: Traumatic brain injury (TBI) remains a main public health problem being associated with high mortality and merbidity. The functional outcome of TBI remains unfavorable despite several surgical and medical therapies. Cerebrolysin is a neuropeptide with potential neuroregenerative entities.

Objective: The aim of the current systematic review and meta-analysis was to investigate the effects of cerebrolysin on functional outcome in patients with moderate and severe TBL.

Data sources: Online databases used included Medline, Scopus, EMBASE, Google Scholar, Web of Science, and Cochrane Library.

Study eligibility criteria: All the relevant studies with randomized clinical trial and cohort design evaluating the effects of intravenous cerebrolysin vs placebo on functional outcome of patients with TBI within the English literature up to October 2018 were included.

Study appraisal and synthesis methods: The articles were reviewed by two independent authors and the data were extracted to a data sheet. P and Cochran's Q-statistics were used to assess heterogeneity. Based on the presence of significant heterogeneity across included studies, data were pooled using random-effects model with Dersimonian-Laird method and presented as standardized mean differences (SMDs) and corresponding 95% CI.

Results: Five articles (5,685 participants) were included in the current meta-analysis. The overall proded findings using random-effects models among partients with TBI indicated that intravenous administration of cerebsolysin significantly increased Glasgow Outcome Scale score (SMD =0.30; 95% CI: 0.18 to 0.42; P<0.001; P<sup>2</sup> 87.8%) and decreased modified Rankin Scale score (SMD =0.29; 95% CI: -0.42 to 0.16; P=0.05; F<sup>2</sup> 89.6%).

Limitations: The results are mainly based on cohort studies and there is a lack of clinical trials in the literature. There is also heterogeneity among the studies regarding the dosage and duration of administration and the measurement of functional outcome.

Conclusion: The results of the current study revealed that intravenous administration of cerebrolysin is associated with improved functional outcome in patients with TBI measured by the Glasgow Outcome Scale and the modified Rankin Scale scores.

Keywords: traumatic brain injury, TBI, cerebrolysin, functional outcome, Glasgow Coma Scale, GOS, modified Rankin Scale, mRS

### Introduction

Traumatic brain injury (TBI) is among the most common public health problems in both developed and developing countries being associated with high mortality and morbidity and heavy disease burden in all age groups. <sup>12</sup> According to Center for Disease Control, TBI has been responsible for ~2.5 million emergency department



Neuropsychiatric Disease and Treatment 2019:15 127-135

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### LITERATURE REVIEW



Intravenous Acetaminophen (Paracetamol) for Postcraniotomy Pain: Systematic Review and Meta-Analysis of Randomized Controlled Trials

Fariborz Ghaffarpasand<sup>†</sup>, Ehsan Dadgostar<sup>‡</sup>, Ghazal llami<sup>‡</sup>, Fatemeh Shoaee<sup>‡</sup>, Amin Niakan<sup>‡</sup>, Sara Aghabaklou<sup>‡</sup>, Maryam Ghadimi<sup>‡</sup>, Sogand Goudarzi<sup>‡</sup>, Maryam Dehghankhalili<sup>‡</sup>, Mohammad Hesam Alavi<sup>‡</sup>

#### Key words

- Acetsminochen
- Craniotomy
- Meta-analysis
  Postoperative pain

#### Abbreviations and Acronyms

CI: Confidence interval

ICU: Intensive care unit

LOS: Length of stay

HCT: Randomized controlled trial SMD: Standardized mean difference

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### INTRODUCTION

Acute pain control after supratentorial craniotomy is considered among the most important indicators of postoperative reovery. Uncontrolled postoperative pain after elective caniotomy will result in patient discomfort, agitation, and increased risk of postoperative complications including increased intrarramial hematoma formation, deep vein thrombosis, and longer duration of intensive care unit (ICU) and hospital stay.<sup>2-st</sup> Currently, the incidence of posternationormy pain in an elective setting has been estimated to range between 65% and 85%.65 Allflough there is an

 BACKGROUND: Acute pain control after supratentorial craniotomy is considered among the most important indicators of postoperative recovery. The aim of this study was to determine the effects of intravenous acetaminophen on postcraniotomy pain.

METHODS: We searched databases including Embase, Scopus, Medline, Cochrane Library, and Web of Science until April 2019. Cochran C test and £ statistic were used to assess the heterogeneity across included clinical trials. Standardized mean difference (SMD) and 95% confidence interval (CI) were used to estimate pooled effect sizes.

RESULTS: Out of 479 reports, 5 randomized controlled trials met the inclusion criteria and were appropriate for our meta-analysis, which included a total of 2635 patients. The pooled results of included clinical trials indicated that paracetamol intake significantly decreased rescue dose (SMD,  $-0.67;\,95\%$  Cl, -1.15 to  $-0.19;\,P<0.01;\,\hat{F}=90.0%), total dosage of rescue (SMD, <math display="inline">-0.78;\,95\%$  Cl, -1.18 to  $-0.37;\,P<0.01;\,\hat{F}=90.0%), intensive care unit length of stay (SMD, <math display="inline">-0.24;\,95\%$  Cl, -0.44 to  $-0.04;\,P=0.01;\,\hat{F}=0.0%), and visual analog scale score (SMD, <math display="inline">-0.16;\,95\%$  Cl, -0.49 to  $-0.00;\,P=0.04;\,\hat{F}=71.7\%)$  and increased patients satisfaction (SMD, 0.28; 95% Cl, 0.14–0.43;  $P<0.01;\,\hat{F}=10.2\%)$  among patients with craniotomy. Time to rescue (SMD, 0.21; 95% Cl, -0.42 to  $0.85;\,P=0.51;\,\hat{F}=94.3\%)$  and hospital length of stay (SMD,  $-0.04;\,95\%$  Cl, -0.24 to  $0.16;\,P=0.69;\,\hat{F}=0.0\%)$  did not significantly change after paracetamol intake.

CONCLUSIONS: The results of this systematic review and meta-analysis indicate that preoperative intravenous administration of acetaminophen is associated with decreased postoperative pain, need for rescue analgesics, and dosages of analgesics after craniotomy surgery.

international consensus regarding optimal posteraniotomy pain control, there is great controversy in treatment options and medical choices; <sup>16,7</sup> Opioids have been shown to provide appropriate pain control after cuantotomy; however, there use is limited in neurocritical care units because of their effects on the fewel of consciousness and neurologic status (detectoration of neurologic status and miosis).<sup>8</sup>

Paracetamol, the intravenous formulation of acetaminophen, has evolved in recent decades for pain control in the acute setting and has been shown to be associated with appropriate pain control and fewer

complications and side effects. 9,50 The drug is available internationally and is a nonopioid agent associated with limited side effects and high bioavailability and long half-life, making it suitable for management of postoperative pain in various settings.11 Several lines of evidence have that intravenous demonstrated acetaminophen reduces the opioid requirement and increases postoperative comfort level. 12,23 However, its efficacy and safety in neurosurgical patients and those undergoing elective craniotomy have been tested in limited studies, among which there are only some randomized controlled trials (RCTs), with

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### Determinants of reoperation after decompressive craniectomy in patients with traumatic brain injury: A comparative study



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#### ARTICLE INFO

Outcome

#### Decompressive craniectomy (DC) Traumatic brain injury (TBI) Reoperation Coagulation Predictive factors

### ABSTRACT

Objectives: Reoperation after decompressive craniectomy (DC) in patients with traumatic brain injury (TBI) remains a dilemma and the risk factors are to be identified. The aim of the current study was to determ determinants and risk factors of reoperation after DC in patients with TBI.

Patients and methods: This retrospective case-controlled study was conducted during a 4-year period from September 2013 to October 2017 in a level I trauma center affiliated with Shiraz University of Medical Sciences in southern Iran. We included all the adult (≥18 years) patients with TBI who underwent primary or secondary DC in our center during the study period. Those who underwent reoperation were compared to those who underwent DC only regarding the demographic findings, clinical features and neuroimaging findings. A univariate and multivariate logistic regression analysis was performed to determine the determining factors of reoperation.

Results: Overall we included 371 patients with mean age of 36.45  $\pm$  14.18 years. Among the patients there were 325 (87.6%) men and 46 (12.4%) women. The reoperation in patients undergoing DC due to TBI was associated with primary DC (p = 0.639) and higher Marshall grade (p = 0.027). Those who underwent reoperation after DG for TBI had significantly higher ICU (p = 0.007) and hospital LOS (p = 0.001) and lower 6month GOSE (p = 0.010). Age (p < 0.001), GCS (p < 0.001) and pupils (p = 0.027) were predictors of outcome in reoperation group. Reoperation in primary DC group was associated with pupil reactivity (p = 0.002) and number of episodes with INR above 1.5 (p = 0.037)

Conclusion: Reoperation after DC for TBI is associated with primary DC, and Marshall grade. The reoperation after DC is associated with worse outcome and longer ICU and hospital stay. The age, GCS and pupil reactivity are the main predictors of outcome in those with reoperation after DC for TBL

### 1. Introduction

Traumatic brain injury (TBI) is a critical public health and socioeconomic problem throughout the world [1-3]. It is the leading cause of mortality and disability among young individuals in high-income countries and the most common cause of mortality and years of potential life lost (YPLL) of individuals between 18 and 44 years in developing countries [4,5]. Worldwide, the incidence of TBI is rising sharply, mainly because of increase in use of motor vehicles in low and middle income countries [1]. TBI will surpass many diseases as the major cause of death and disability by the year 2020 [6]. It is often referred to silent epidemic [7]: silent insofar as patients are not vociferous because of the invisibility of symptoms and low awareness of the chronicity of its sequelae and insofar as society in general is largely unaware of the magnitude of the problem.

Decompressive craniectomy (DC) is among the available surgical treatments in patients with TBI suffering from intracranial evacuatable pathologies (primary DC) or refractory intracranial hypertension (secondary DC); however, its role in decreasing mortality and morbidity is controversial which is subjected to large scale randomized clinical trials

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Editorial

Bull Emerg Trauma 2020;8(2):53-55





### Tranexamic Acid; A Glittering Player in the Field of Trauma

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Trauma is still the leading cause of mortality and morbidity worldwide with an estimated 5.8 million mortalities every year [1] and approximately 60 million traumatic brain injuries (TBI) annually [2]. Hemorrhage remains the most common preventable cause of mortality and morbidity following trauma either in civilian or military settings [3, 4]. Intracranial bleeding following TBI results in increased intracranial pressure (ICP). brain herniation and cerebral edema which are all secondary insults to the brain parenchyma leading to increase disability and mortality [5]. Thus, the development and administration of antifibrinolytic agents have been the focus of traumatic injuries during the previous decades with the hypothesis of hemorrhage cessation and hemostasis with a medical agent rather than a surgical intervention. These efforts resulted in developing several agents and subsequent large multicenter clinical trials to define the best antifibrinolytic agent for prevention of death following TBI.

Tranexamic acid (TXA), an antifibrinolytic agent being introduced in 1962, has been spotlight of the TBI treatment during the past decade [6]. TXA provides its antifibrinolytic effects through binding to the plasminogen molecule which in turns blocks connection of the plasminogen to the plasmin and fibrin. These cascades lead to stabilization of the formed network through secondary hemostasis. The drug is administered through oral and intravenous routes and has a bioavailability of 33 and 90% respectively [7]. Several applications have been approved for the TXA including the trauma, obstetrics and gynecology condition (menstrual bleeding, obstetrics bleeding), orthopedics surgery, spinal surgeries, dental procedures, hemoptysis, hemophilia, and epistaxis [6, 8, 9].

Until now, several studies have addressed the effects of the TXA on the patients with trauma with an emphasis on the TBI [10-12]. The two main projects accordingly include the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage (CRASH) [10, 11] and Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) [13]. Very recently, the results of the CRASH-3 was published which provides the highest level of evidence regarding the efficacy and safety of the TXA in patients with TBI [10]. In addition, several lines of recent evidence have demonstrated that pre-hospital and early administration of TXA leads to clot stabilization and a reduction of fibrinolytic activity, causing a decrease in fibrin degradation products buildup (D-dimer) [14] which in turn is associated with prolonged time to death and significantly improved early survival [15].

We herein, discuss and summarize the results of these three main studies in order to emphasis on

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### Risk Factors of Neural Tube Defects in a Sample of Iranian Population from Southern Iran; A Hospital-Based Investigation

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Background and Aim: The risk factors of the neural tube defects (NTD) have been previously described but there are ethnic and geographical variations. Data from Iranian population is still scarce. The objective of the current study was to investigate the NTDs risk factors in a large sample of Iranian patients admitted to a single center.

Methods and Materials/Patients: This case-control study was performed within five years from 2012 to 2017 in Namazi Hospital of Shiraz, a tertiary referral center for neomatal anomalies in south of Iran Onehundred newboms with NTDs were included in the study as the case group and 200 healthy newboms as the control group. We recorded the baseline characteristics including the maternal variables (age, weight, height, previous pregnancy and gravidity, gestational age), newborn information (birth weight, clinical diagnosis, clinical finding in examination, and clinical finding in radiologic test) and medical history of the perinatal

Results: The baseline characteristics of the mothers were matched in both goups NTDs were associated with lower folio and intake during pregnancy (66% vs. 78%, p=0.030, OR95% Cl=1.82) and before pregnancy (p=0.002, OR95% Cl=2.35). The prevalence of nevral tube defeates was significantly higher in patients who lived in hot climates (p=0.001).

Conclusion: Taking adequate folic acid supplement before and during pregnancy can reduce the risk of NTDs in Iranian population. Hot climate zones were associated with increased risk of NTDs in Iran. Keywords: Neural Tube Defect, Risk Factors; Folic Acid; Geographic Distribution

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Highlights

. Taking adequate folic acid supplement before and during pregnancy can reduce the risk of NTDs in Iranian population.

. Hot climate zones were associated with increased risk of NTDs in Iran

The risk factors of the neural tube defects (NTD) have been previously described but there are ethnic and geographical variations. Data from the Iranian population are still scarce. In the current study, we included a total number of 100 newborns with NTDs and 200 healthy newborns. The baseline characteristics including the maternal variables (age, weight, height, previous pregnancy and gravid, gestational age), newborn information (birth weight, clinical diagnosis, clinical findings in examination, and clinical findings in radiologic test) and medical history of the perinatal period were recorded and compared between the two study groups. We found that NTDs were associated with lower folic acid intake during pregnancy and before pregnancy. The prevalence of neural tube defects was significantly higher in patients who lived in hot climates. We concluded that taking adequate folic acid supplement before and during pregnancy can reduce the risk of NTDs in Iranian population. Hot climate zones were associated with increased risk of NTDs in Iran.



### **Editorial:**



### Ventrolateral Preoptic Nucleus of Hypothalamus: A Possible Target for Deep Brain Stimulation for Treating Sexual Dysfunction

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### Keywords:

Ventrolateral Preoptic Nucleus (VLPO), Hypothalamus, Sexual orientation

### ABSTRACT

Sexual function and orientation is a complex platform of human personality which is being modulated by several brain circuities which is less understood currently. Recently, several studies have demonstrated interesting results regarding the role of several brain locations in sexual behaviors and orientation. Sexual arousal in homosexual men are associated with activation of the left angular gyrus, left caudate nucleus, Ventrolateral Preoptic (VLPO) Nucleus of Hypothalamus and right pallidum; while it is associated with bilateral lingual gyrus, right hippocampus, and right parahippocampal gyrus in heterosexual men. We postulate that sexual-orientation behaviors are being mediated by several circuits in the brain in the center of which the VLPO is playing an indistinguishable role. We hypothesize that the different aspects of the sexual dysfunction could be associated with innate or acquired lesions of VLPO. Accordingly, the electrical stimulation of the nucleus in those with sexual dysfunction would be a treatment option. Thus the VLPO could be considered a target for Deep Brain Stimulation (DBS) in individuals with impaired sexual function.

he basic neuroscientific infrastructure of the sexual orientation and the gender disorders have been the matter of several studies without clear evidence and physiology [1]. Recently, Epprecht et al. [2] have addressed an important issue in patients with Subarachnoid Hemorrhage (SAH) which affects the quality of life to a great extent. The results of this study demonstrated that sexual dysfunction is a common problem

even after good grade SAH. Decreased sexual desire and loss of orgasmic experience were among the most common reported problems. The results of this study along with our own experience and other lines of evidence, lighted up an idea regarding the sexual function and sexual orientation.

Sexual function and orientation is a complex platform of human personality which is being modulated by sev-

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### MicroRNA-199a Upregulation Mediates Lumbar Intervertebral Disc Degeneration and is Associated with Clinical Grades of Degeneration

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### ABSTRACT

AIM: To determine the expression profile of miRNA-199a-5p in intervertebral disc degeneration (IDD) and its correlation to the grade of IDD

MATERIAL and METHODS: This case-controlled study was conducted during a 6-month period from 2017 to 2018 in two university hospitals in Shiraz, Iran. We included 15 patients with grade 3 and 4 of Pfirmann and 5 patients with traumatic lumbosacral fractures with grade I. Total discectomy was performed in all the individuals and the samples were sent to the laboratory. The nucleus pulposus (NP) cells were isolated and the RNA was extracted, cDNA was synthesized by reverse transcriptase and the expression was measured using real-time polymerase chain reaction (RT-PCT).

RESULTS: We overall included 20 patients in two study groups. Both study groups were comparable regarding the baseline and clinical characteristics except for age (p=0.026). The fold change (p=0.007), and relative expression (p=0.012) of the miRNA-199a-5p was found to be significantly higher in patients compared to controls. The fold change (p=0.001), and relative expression (p<0.001) were also associated with the Pfirmann grading. We found that the area under curve (AUC) was 0.880 (95%CI: 0.721-0.938) indicative of moderate accuracy

CONCLUSION: Expression of the miRNA-199a-5p is increased in the IDD. The expression of the miRNA-199a-5p was also associated with the grade of the degeneration based on the Pfirmann grading

KEYWORDS: Intervertebral disc degeneration, MicroRNA-199a, Target genes, Pfirrmann grade

### INTRODUCTION

"ntervertebral disc degeneration (IDD) is currently considered the etiology of low back pain (LBP) which is the second most common complain of the patients referring to the outpatient clinics worldwide (12). LBP is associated with high disease burden and disability worldwide. According to the global burden of the disease, LBP ranked highest in terms of

disability (YLDs), and sixth in terms of overall burden (DALYs) with a global prevalence of 9.4% in 2010, increasing with age (6). There are several key steps identified in IDD which includes loss of extracellular matrix, endplate cartilages hyperplasia and subsequent scierosis, loss of height and release of pro-inflammatory cytokines (19,24). The nucleus pulposus (NP) cells are cartilage-like cells with minimal regenerative

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This study has been presented at the 26th International Student Congress of (bio) Medical Sciences (ISCOMS 2019) between 3 and 7 June 2019 at Leiden Netherlands



Turk Neurosurg, 2019



Original Investigation

### Determination of miRNA-199a and its Target Genes in Degenerative Lumbar Intervertebral Disc

Majid Reza FARROKHI¹, Mohammad Hossein KARIMI³, Fariborz GHAFFARPASAND³, Masih SHERAFATIAN⁴

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"Tarbiat Modares University, Faculty of Biological Sciences, Department of Molecular Genetics, Tehran, Iran

This study has been presented as at the 29th International Student Congress of (bit) Medical Sciences (ISCOMS 2019) between 3 and 7 June 2019 at Leiden, Netherlands.

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### ABSTRACT

AIM: To determine the expression profile of miRNA-199a-5p in intervertebral disc degeneration (IDD) and its correlation to the grade of IDD.

MATERIAL and METHODS: This case-controlled study was conducted during a 6-month period from 2017 to 2018 in two university hospitals in Shiraz, Iran. We included 16 patients with grade 3 and 4 of Pfirmann and 5 patients with traumatic lumbosacral fractures with grade I. Total discoctomy was performed in all the individuals and the samples were sent to the laboratory. The NP cells were isolated and the RNA was extracted. CDNA was synthesized by reverse transcriptase and the expression was measured using real-time polymerase chain reaction (RT-PCT).

RESULTS: We overall included 20 patients in two study groups. Both study groups were comparable regarding the baseline and clinical characteristics except for age (p=0.026). The fold change (p=0.007) and relative expression (p=0.012) of the miRNA-199a-59 was found to be significantly higher in patients compared to controls. The fold change (p=0.001) and relative expression (p=0.001) were also associated with the Pfirmann grading. We found that the area under curve (AUC) was 0.880 (95%CI: 0.721-0.938) indicative of moderate accuracy.

CONCLUSION: Expression of the miRNA-199a-5p is increased in the IDD. The expression of the miRNA-199a-5p was also associated with the grade of the degeneration based on the Pfirmann grading.

KEYWORDS: Intervertebral disc degeneration, MicroRNA-199a, Target genes, Pfirrmann grade

### **■ INTRODUCTION**

Intervertebral disc degeneration (IDD) is currently considered the etiology of low back pain (LBP) which is the second most common complain of the patients referring to the outpatient clinics worldwide (12). LBP is associated with high disease burden and disability worldwide. According to the global burden of the disease, LBP ranked highest in terms of disability (YLDs), and sixth in terms of overall burden (DALYs) with a global prevalence of 9.4% in 2010, increasing with

age (6). There are several key steps identified in IDD which includes loss of extracellular matrix, endplate actifiages hyperbasia and subsequent solerosis, loss of height and release of pro-inflammatory cytokines (19,24). The nucleus pulposus (NP) cells are cartiage-like cells with minimal regenerative potentials which maintain the interverterbal disc function and structure (1). The apoptosis and senescence of the NP cells is considered the key step in IDD and understanding the factors contributing to NP cell apoptosis will shed light on the

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CLINICAL ARTICLE

### Clinical outcome of V-Y flap with latissimus dorsi and gluteal advancement for treatment of large thoracolumbar myelomeningocele defects: a comparative study

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OBJECTIVE Surgical repair and closure of myelomeningocole (MMC) defects are important and vital, as the mortality receives it as thigh as 65%—70% in untreated patients. Closure of large MMC defects is challenging for pediatric neurosurgeons and plastic surgeons. The aim of the current study is to report the operative characteristics and outcome of a series of Iranian patients with large MMC defects utilizing the V-Y flap and with latissimus dorsi or gluteal muscle advancement.

METHODS This comparative study was conducted during a 4-year period from September 2013 to October 2017 in the pediatric neurosurgery department of Shira: Namazi Hospital, Southern Iran. The authors included 24 patients with large MMC defects who underwent surgery utilizing the bilateral V-Y flap and latissimus dorsi and gluteal muscal edvancement. They also retrospectively included 19 patients with similar age, sex, and defect size who underwent surgery using the primary or delayed closure techniques at their center. At least 2 years of follow-up was conducted. The frequency of leakage, necrosis, dehiscence, systemic infection (sepsis, pneumonia), need for ventriculoperitoneal shunt insertion, and mortality was compared between the 2 groups.

RESULTS The bilateral V-Y flap with muscle advancement was associated with a significantly longer operative duration ( $\rho$  < 0.001) than the primary closure group. Those undergaing bilateral V-Y flaps with muscle advancement had significantly lower rates of surgical site infection ( $\rho$  = 0.038), wound dehiscence ( $\rho$  = 0.013), and postoperative CSF leakage ( $\rho$  = 0.030) than those undergoing primary repair. The bilateral V-Y flap with muscle advancement was also associated with a lower mortality rate ( $\rho$  = 0.038, OR 5.09 (95% Cl. 1/2-23.1)) than primary closure. In patients undergoing bilateral V-Y flap and muscle advancement, a longer operative duration was significantly associated with mortality ( $\rho$  = 0.008) in addition, surgical site infection ( $\rho$  = 0.032), wound dehiscence ( $\rho$  = 0.011), and postoperative leakage ( $\rho$  = 0.011) were predictors of mortality. Neonatal sepsis ( $\rho$  = 0.002) and postoperative NEC ( $\rho$  = 0.011) were among other predictors of mortality in this group.

CONCLUSIONS The bilateral V-Y flap with latissimus dorsi or gluteal advancement is a safe and effective surgical approach for covering large MMC defects and is associated with lower rates of surgical site infection, dehiscence, CSF leakage, and mortality. Further studies are required to elucidate the long-term outcomes.

https://theins.org/doi/abs/10.3171/2019.1.PEDS18232

KEYWORDS myelomeningocele; V-Y flap; latissimus dorsi muscle; gluteal muscle; clinical outcome; congenital

MEGICAL repair and closure of myelomeningocele (MMC) defects is important and vital, as the mortality rate is as high as 65%-70% in untreated patients. The aim of surgical repair is to protect the neural elements by placing them in the thecal sac, stop the CSF leakage, and decrease the rate of meningitis and infec-

tion 3.10 Limited and small defects can be closed and repaired primarily, while closure of large defects remains a challenge for neurosurgeons and plastic surgeons. Large thoracolumbar defects are associated with high mortality and morbidity, and their closure and coverage have been the subject of several research investigations. To date, sev-

ABBREVIATIONS MMC = myelomeningocele; NEC = necrotizing enterocolitie; SSI = surgical site infection; VP = ventriculoperitoneal. SUBMITTED April 18, 2018. ACCEPTED January 31, 2019.

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J Neurosurg Pediatr April 19, 2019

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#### LETTER TO THE EDITOR

In Reply to "Noncoding Ribonucleic Acid Studies of Lumbar Disk Disease: Decade Retrospect"



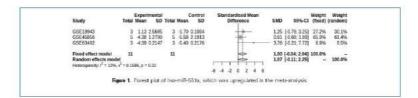
We have read with interest the letter to the editor by Wang' regarding our recently published article in WORLD NEUROSURGERY entitled "MicroRNA Expression Profiles, Target Genes and Pathways in Intervertebral Disk Degeneration; A Meta-Analysis of 3 Microarray Studies."2 In this meta-analysis we have included 3 microazray studies, which included nucleus pulposus (NP) cells of normal and degenerated intervertebral disks. 245 Zhao et al? included so natients with herniated lumbar disks as the case group and 20 patients with traumatic injuries of the lumbar spine as the control group. In the study by Wang et al,1 6 patients with intervertebral disk degeneration (IDD) were included as cases and 6 patients with idiopathic scoliosis undergoing anterior release as controls. Lan et al2 and Liu et al4 included 5 patients with IDD and 5 cadaveric donors with normal disks as the control group. Wang' raised some concerns regarding the heterogeneity of the data used in our meta-analysis. He believes that there are 3 separate types of heterogeneity in the current study: 1) microarray control samples derived from different scenarios including scoliosis, trauma, and cadaveric disks; 2) total ribonucleic acids (RNAs) were extracted from tissues or isolated cells; and 3) microarray studies were performed with different micro RNA (miRNA) versions. These existing differences may result in risks of bias for result interpretation. He also recommended performing heterogeneity testing to decrease bias in the results.

Studies in a systematic review are inevitably different. Heterogeneity in a systematic review can be defined as any kind of variability among collected studies. Variability in the pacticipants, the study design, or the outcomes cause clinical, methodologic, and statistical heterogeneity, respectively. <sup>18</sup> In this article we discuss the heterogeneity in our meta-analysis of IDD. <sup>2</sup> We address 2 main types of heterogeneity in our meta-analysis of microarray studies in IDD: clinical and statistical heterogeneity. <sup>2</sup> The NP cells used in these microarray studies were derived from different scenarios including the scotlosis, trauma, and cadaveric disks. Alfhough these might have different natures, they are all considered normal NP cells. The normality of the disk tissue and NP cells is defined according to the stundard raddologic criteria, which is a defined according to the stundard raddologic criteria, which is

Pfirmann grading. The Pfirmann classification was used to classify the grade of degeneration in all the included studies. Grades 3 and 4 of Pfirmann classification were considered as disk degeneration while grades 1 and 2 were considered as the healthy disks. Thus there have been inclusion criteria regarding the type and extent of the degeneration in included disks. In other words, although the nature of the included samples is different, they share similar radiologic characteristics and grades of degenerations. This explains the clinical heterogeneity of the meta-analysis.

For evaluating the statistical consistency of our meta-analysis results, we calculated the heterogeneity for all 5 differentially expressed miRNAs found in this study and visualized the forest plot for 2 of these miRNAs: 1 upregulated (Figure 1) and 1 downregulated miRNA (Figure 2). As commonly practiced,10 we assessed the statistical heterogeneity in our study by measuring 12-statistic and drawing forest plots. 12 was calculated for all miRNAs, which were previously identified as differentially expressed in the results of our meta-analysis. These miRNAs were miR-199a-5p, miR-574-3p, miR-551a, miR-640, and miR-483-5p. All of the calculated I' values corresponded to low heterogeneity, and none of the P values were significant (P < 0.05). Therefore we deduced that the statistical heterogeneity in our study was nonsignificant. With the help of the meta packagers in R environment (The R Foundation for Statistical Computing, http://www.r-project.org/foundation), detailed forest plots of miR-5512 and miR-483-5p were depicted in Figures 1 and 2, respectively.

Overall, interest in the pathogenesis of IDD is increasing every and this leads to our increased knowledge of the disease pathogenesis. By elucidating the miRNA mechanisms of the IDD, we can probably establish appropriate treatment and preventive strategies for IDD. Thus, meta-analysis of microarray studies in this field could help determine a significant cause of degeneration in intervertebral disks and guide further research based on their results. The heterogeneity in the current study was not significant and thus the results could be interpreted. However, the clinical and statistical heterogeneity should always be kept in mind when performing such meta-analysis.







### LITERATURE REVIEW



MicroRNA Expression Profiles, Target Genes, and Pathways in Intervertebral Disk Degeneration: A Meta-Analysis of 3 Microarray Studies

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#### Key words

- Expression
- Intervertebral disk degeneration
- Meta-analysis
- MicroRNA
- Target gene
- Abbreviations and Acronyms

AF: Annulus fibrosis

ECM: Extracellular matrix

GO: Gene Ontology

IDD; Intervertebral disk degeneration LBP: Chronic low back pain

miRNA: MicroRNA

NP: Nucleus pulposus

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### INTRODUCTION

With over 600 million individuals afflicted, chronic low back pain (LBP) is the leading cause of years lived with disability worldwide."3 At any given moment, an estimated 12% of the global population suffers from LBP. The prevalence of LBP reaches 38% annually,+ and lifetime prevalence has been reported to be as high as 80%.5 The effective management of LBP consequently requires an in-depth understanding of both the normal structure and function of the lumbar spine and the pathophysiologic changes that arise disease." with degenerative The relationship of LBP to intervertebral disk

- BACKGROUND: Determining the expression profile and target genes of microRNA (miRNA) would assist in determining the pathophysiologic pathways in intervertebral disk degeneration (IDD). The aim of this study was to determine the expression profile of miRNA in degenerated intervertebral disks compared with normal healthy intervertebral disks.
- METHODS: We conducted a meta-analysis of 3 available miRNA expression datasets to identify a panel of co-deregulated miRNA genes and overlapping biological processes in IDD. Degenerated intervertebral disks were compared with normal healthy disks. We selected 35 miRNA features common to all 3 platforms. Then, we calculated differential expression P values from our unpaired data using metaMA package in R statistical software according to the moderated t test method (Limma). Based on the P values (where the threshold was <0.05), a list of differentially expressed miRNAs was identified,
- RESULTS: After normalization and selection of common miRNA features across all 3 platforms, we found a total of 5 differentially expressed miRNAs, among which miR-574-3p, miR-199a-5p, and miR-483-5p were not identified in any individual studies. Our results revealed that miR-199a-5p, miR-574-3p, miR-551a, and miR-540 are commonly upregulated in IDDs compared with control disks, whereas miR-483 is commonly downregulated. Pathway analysis of identified dysregulated miRNAs indicated the involvement of extracellular matrix-receptor interaction, adherens junction, and transforming growth factorbeta signaling pathway in the pathogenesis of IDDs. Moreover, the network of predicted targets for these miRNAs identified most affected target genes as ERBB4 and CLTC.
- CONCLUSIONS: We found that the identified miRNAs through meta-analysis are candidate predictive markers for IDDs through different pathways.

degeneration (IDD) remains poorly understood. 5.8 Symptomatic diel Symptomatic degeneration is frequently accompanied aberrant neurovascular ingrowth within the nucleus pulposus (NP) and annulus fibrosis (AF).9 A regional immune response is elicited by structural changes such as annular tears.11 The resulting formation of vascularized granulation tissue evokes release of cytokines, including interleukin-6 and interleukin-8 and prostaglandin E2.22 These inflammatory mediators are proposed to sensitize local nociceptors, thereby lowering pain thresholds." Hypermobility of the intervertebral disk

occurs in conjunction with these structural and biomechanical changes. As a consequence, the biomechanics of the lumbar spine are altered, with the loading of facet joints, ligaments, and paraspinal musculature producing potent generators of pain.7

Micro-RNAs (miRNAs) are noncoding small-size RNA molecules of 20-22 nucleotides in length, which play an important role in transcription regulation of various genes in humans. They account for 1%-3% of the human genome, and up to 30% of the proteins in the human body are regulated by miRNAs. The function of miRNAs is executed by

### **IV** TRANSPLANTATION

### Review of Renal Biopsies, A Single Center Experience

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Keywords, kidney diseases, lupus nephritis, membranous glomerulonephritis, primary glomerulonephritis, secondary glomerulonephritis

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No large study has been conducted on biopsy-proven nephropathies. Our aim was to report clinical and pathological pattern of kidney disease diagnosed by kidney biopsy in our center.

This is a retrospective study on kidney biopsy during 7 years, we analyzed the results of kidney biopsies and their clinical data. Data were analyzed by SPSS 18.0 and a P < .05 was considered. In 1355 kidney biopsies (55.7% women, age = 33.2  $\pm$  16.4), primary glomerulonephritis (GN) was the main feature (57.1%). The most common presentation was asymptomatic urine abnormality (32.3%). Lupus nephritis (24.5%), membranous GN (17.0%), and focal segmental glomerulosclerosis (13.9%) were the most frequent diagnosis.

This study highlights the histopathological patterns of kidney disease in southern Iran. lupus nephritis, membranous GN, and focal segmental glomerulosclerosis are currently the three major diseases. These results have an important role in organizing renal health plans as an initial phase in our population.

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### INTRODUCTION

Clinical and pathologic data about kidney disease provides important information. <sup>1-5</sup> Some studies of renal diseases in Western countries are existing from kidney biopsy registries. <sup>6</sup> Several kidney biopsy registries in some countries are available, showing comparable trends in incidence and prevalence of kidney diseases. <sup>7-6</sup> In contrast, few reports provide detailed data for kidney diseases in the Middle East. <sup>6</sup> The essential of kidney diseases studies is felt in other regions due to kidney diseases differences in various regions that may arise from the diversity in prevalence of infectious diseases, social/economic status in indication for biopsy, environmental exposure, and socio-economic status. <sup>1-6,9</sup>

In previous papers, we have described a high frequency of chronic kidney disease and dialysis population in our center among different age groups. <sup>10-12</sup> There is a lack of systematic data of renal disease from our country over a long period of time that indicated the needs and usefulness of these studies in this regard.

The aim of this study was to describe the clinical and histopathological patterns of kidney disease diagnosed by kidney biopsy during a period of 7 years in Fars province, Sothern Iran.

### MATERIALS AND METHODS General Data

This is a retrospective study that was performed on renal diseases in native kidneys diagnosed by a biopsy since January of 2011 to December of 2017, from the center of nearly 5 million people, from Fars province, Sothern Iran, by the same pathologist, including the available clinical, laboratorial and histological parameters. A total of 1355 renal biopsies were performed.

### **Histopathological Data**

Biopsies were evaluated by light microscopy and/or electron microscopy (EM). All biopsy





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### Determinants of reoperation after decompressive craniectomy in patients with traumatic brain injury: A comparative study



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#### ARTICLE INFO

Emmonde Decompressive craniectomy (DC) Traumatic brain injury (TBI) Reoperation Coagulation Predictive factors Outcome

#### ABSTRACT

Objectives: Reoperation after decompressive craniectomy (DC) in patients with traumatic brain injury (TBD) remains a dilemma and the risk factors are to be identified. The aim of the current study was to determine the determinants and risk factors of reoperation after DC in patients with T8L

Patients and methods: This retrospective case-controlled study was conducted during a 4-year period from September 2013 to October 2017 in a level I trauma center affiliated with Shiraz University of Medical Sciences in southern Iran. We included all the adult ( > 18 years) patients with TBI who underwent primary or secondary DC in our center during the study period. Those who underwent reoperation were compared to those who underwent DC only regarding the demographic findings, clinical features and neuroimaging findings. A univariate and multivariate logistic regression analysis was performed to determine the determining factors of reoperation

Results: Overall we included 371 patients with mean age of 36.45 ± 14.18 years. Among the patients there were 325 (87.6%) men and 46 (12.4%) women. The reoperation in patients undergoing DC due to TBI was associated with primary DC (p = 0.039) and higher Marshall grade (p = 0.027). Those who underwent reoperation after DC for TBI had significantly higher IGU (p = 0.007) and hospital LOS (p = 0.001) and lower 6month GOSE (p = 0.010). Age (p < 0.001), GCS (p < 0.001) and pupils (p = 0.027) were predictors of outcome in reoperation group. Reoperation in primary DC group was associated with pupil reactivity (y = 0.002) and number of episodes with INR above 1.5 (p = 0.037)

Conclusion: Reoperation after DC for TBI is associated with primary DC, and Marshall grade. The reoperation after DC is associated with worse outcome and longer ICU and hospital stay. The age, GCS and pupil reactivity are the main predictors of outcome in those with reoperation after DC for TBI.

### 1. Introduction

Traumatic brain injury (TBI) is a critical public health and socioeconomic problem throughout the world [1-3]. It is the leading cause of mortality and disability among young individuals in high-income countries and the most common cause of mortality and years of potential life lost (YPLL) of individuals between 18 and 44 years in developing countries [4,5]. Worldwide, the incidence of TBI is rising sharply, mainly because of increase in use of motor vehicles in low and middle income countries [1]. TBI will surpass many diseases as the major cause of death and disability by the year 2020 [6]. It is often referred to silent epidemic [7]: silent insofar as patients are not vociferous because of the invisibility of symptoms and low awareness of the chronicity of its sequelae and insofar as society in general is largely unaware of the magnitude of the problem.

Decompressive craniectomy (DC) is among the available surgical treatments in patients with TBI suffering from intracranial evacuatable pathologies (primary DC) or refractory intracranial hypertension (secondary DC): however, its role in decreasing mortality and morbidity is controversial which is subjected to large scale randomized clinical trials

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Applied Magnetic Resonance

#### ORIGINAL PAPER



# Synthesis, Characterization and MRI Application of Cobalt-Zinc Ferrite Nanoparticles Coated with DMSA: An In-vivo Study

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#### Abstract

The aim of this study was to synthesize and characterize the dimercaptosuccinic acid (DMSA) cobalt–zinc (Co–Zn) ferrite magnetic nanoparticles (NPs) and their efficiency as a contrast agent in in vivo MR imaging of rat liver. Co–Zn ferrite NPs were synthesized by the thermal decomposition method and stabilized by DMSA. The NPs were characterized by different analyses to study their physical and magnetic properties and were injected into 6 adult male rats. Liver MRI was performed to measure the signal intensity at different times. The average nanoparticle size was estimated at about  $8\pm1$  nm using transmission electron microscopy (TEM). The  $r_2$  and  $r_2*$  relaxivity of these particles were obtained at 32.85 and 168.96 mmol  $L^{-1}$  s<sup>-1</sup>, respectively, using an agarose phantom imaged by MRI. In the in vivo condition, injection of SNPs (2.5 mg Fe/kg) showed negative contrast in a way that for  $T_2$  and  $T_2*$  weighted the maximum contrast enhancement was 58.46 and 77.13%, respectively. Regarding our results, the synthesized Co–Zn ferrite NPs stabilized by DMSA are appropriate agents for increasing the contrast in both  $T_2$  and  $T_2*$  weighted based on MR imaging in rat liver.

### 1 Introduction

Magnetic resonance imaging (MRI) has been a powerful technology as a diagnostic method for in vivo assessment of diseases with high resolution [1]. Enhancing the tissue contrast of the images obtained from this technique by adding extrinsic agents has become the necessary process for lots of patients. Magnetic NPs are widely used as

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## Medical image registration using deep neural networks: A comprehensive review \*



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#### ABSTRACT

Image-guided interventions are saving the lives of a large number of patients where the image registration should indeed be considered as the most complex and complicated issue to be tackled. On the other hand, a huge progress in the field of machine learning has recently made by the possibility of implementing deep neural networks on the contemporary many-core CPUs. It has opened up a promising window to challenge with many medical applications in more efficient and effective ways, where the registration is not an exception. In this paper, a comprehensive review on the state-of-the-art literature known as medical image registration using deep neural networks is presented. The review is systematic and encompasses all the related works previously published in the field. Key concepts, statistical analysis from different points of view, confining challenges, novelties and nain contributions, key-enabling techniques, future directions, and prospective trends all are discussed and surveyed in details in this comprehensive review. This review allows a deep understanding and insight for the readers active in the field who are investigating the state-of-the-art and seeking to contribute the future literature.

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### 1. Introduction

In most medical interventions, there are a number of cases in which some images need to be captured for diagnosis, prognosis, treatment, and follow-up purposes. These images can vary in terms of temporal, spatial, dimensional, or modular. Image fusion causing information synergy can have a significant contribution to guide and support physicians in the process of decision making, mostly in an online and real-time fashion. Lack of alignment is unavoidable for these images taken at different times, conditions, and setups; hence, can challenge the quality and accuracy of the subsequent analyses. Image registration is the process of aligning two (or more) given images based on an identical geometrical coordination system. The aim is at finding an optimum spatial transformation that registers the structures-of-interest in the inputted images in the best way. This problem is important in numerous ways in the field of machine vision e.g. for remote sensing, object tracing, satellite imaging, and so on [1].

Image registration is also fundamental to the image-guided intervention where e.g. telesurgery, Image-Guided Radiotherapy (IGRT), and precision medicine cannot be operational without the proper utilization of image registration techniques

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