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Pulse surgical automation platform; Nuvasive Inc.

Nuvasive, Siemens partner for novel surgical tech integrations for spine procedures

By Stacy Lawrence, Staff Writer

Minimally invasive spine surgery player Nuvasive Inc. has partnered with imaging giant Siemens Healthineers AG to develop new approaches to integrating the 3D imaging, navigation and surgical automation used in spine surgery. The pair aim to improve workflow efficiency and precision delivery for minimally invasive spine surgery technology in the operating room.

The first project will be to integrate the newly cleared Pulse surgical automation platform from San

See Nuvasive, page 5

Inside

China's device classification catalog should streamline new product categorization

By Elise Mak, Staff Writer

HONG KONG – China's new medical device classification catalog took effect on Aug. 1, one year after the draft was published by the China National Drug Administration (CNDA). Classifying and registering devices have now become easier,

See China, page 6

Australia seeks industry input to shape policy on SaMD, device cybersecurity

By Tamra Sami, Staff Writer

PERTH, Australia – Australia's TGA is asking for industry input to shape policy on software as a medical device (SaMD) and cybersecurity for medical devices (CSfMD).

The agency said that in the SaMD arena, new

See Australia, page 7

Legislation to reform IVD regs is gaining momentum on Hill

By Mark McCarty, Regulatory Editor

The need to overhaul the FDA's regulation of in vitro diagnostics generally and lab-developed tests in particular is a matter of some standing, but there are signs that legislation may soon be moving on Capitol Hill. The impetus this time is to some extent abetted by a technical assistance document drafted by the FDA, which among other

See IVDs, page 8

Startup aims to evolve feeding tube insertion as it works toward FDA nod

By Liz Hollis, Staff Writer

Inserting feeding tubes is a common practice, but patients often have to go to the surgical suite for them to be placed. A Baltimore startup is looking to change this situation with its Point-of-care Ultrasound Magnet Aligned (PUMA) system.

"It's at the stage now where it's incredibly real and about to go into patient care," Howard Carolan, co-founder and CEO of Coaptech LLC, told *BioWorld MedTech*. "We don't think anyone else has this. It's a way to do it immediately . . . at the bedside, with the presiding team." He noted that

See Coaptech, page 9

Cancer cell lines' evolution affects drug response, and everything else

By Nuala Moran, Staff Writer

It's not news that human cancer cell lines evolve over time, but the extent to which they diverge and the implications that has for the reproducibility of preclinical research and drug screening have now been laid bare in a genomic

See Cancer, page 10

BioWorld MedTech's Neurology Extra

Production Editor Andrea Applegate on one of med-tech's key sectors

Read this week's edition

Other news to note

Premier Inc. of Charlotte, N.C., entered a partnership with **Progknowse Inc.** of McLean, Va., for development of clinical and genomic datasets for use with the former's Premier Connect performance improvement platform. The datasets will provide predictive analytics capabilities that support precision medicine and personalized care delivery. The analytics will be based on a de-identified data set that includes clinical outcomes on roughly 45 percent of all U.S. hospital discharges.

Financings

Co-Diagnostics Inc., a Salt Lake City-based molecular diagnostics company, reported the closing of a non-convertible debt instrument for $2 million. The company will apply the incoming funds towards working capital, to expand distribution of its infectious disease testing products, and to accelerate initiatives to develop multiplex screens for liquid biopsy cancer screening, blood-bank screening and single nucleotide polymorphism detection.

Daily M&A

Specialtycare Inc., a Brentwood, Tenn.-based provider of outsourced intraoperative neuromonitoring (IONM), perfusion and surgical services, said it has acquired IONM provider **Precedent Health Inc.**, also of Brentwood, Tenn. With Precedent Health, Specialtycare increases the number of associates available to support cases in our existing markets across the U.S. while adding significant new coverage in markets such as Buffalo, N.Y.; New York; Detroit; and Portland, Ore. The company employs more than 500 IONM professionals, supporting over 100,000 procedures annually for more than 725 IONM customers and 2,300 surgeons. Financial terms of the acquisition were not disclosed.

Appointments and advancements

Grail Inc. of Menlo Park, Calif., reported Aug. 8 it had added Hal Barron and Hans Bishop to the company's board. Barron is the CSO and president of R&D at Glaxosmithkline, while Bishop was the founder, president and CEO of Juno Therapeutics.

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BioWorld MedTech stock report for public med-tech companies

Company	Symbol	Close 8/3	Close 8/10	Change Week	Change YTD	Vol (000)
Abbott Labs	ABT	65.23	64.03	-1.84	12.20	13780
Abiomed	ABMD	377.11	377.83	0.19	101.61	1656
Accelerate Dx	AXDX	21.40	22.25	3.97	-15.08	1394
Accuray	ARAY	3.80	3.85	1.32	-10.47	1214
Agilent Tech	A	65.73	66.26	0.81	-1.06	8377
Align Tech	ALGN	363.51	364.53	0.28	64.06	1982
Allergan	AGN	185.93	184.00	-1.04	12.48	5529
Allied Healthcare	AHPI	2.35	2.36	0.43	12.92	9
Allscripts	MDRX	13.85	13.70	-1.08	-5.84	6792
Alphatec	ATEC	2.87	3.24	12.89	21.80	564
Angiodynamics	ANGO	21.69	21.35	-1.57	28.38	365
Anika Therapeutics	ANIK	41.33	41.40	0.17	-23.21	345
Antares Pharma	ATRS	2.60	2.90	11.54	45.73	7287
Apollo Endosurgery	APEN	8.55	7.74	-9.47	38.21	337
Athenahealth	ATHN	149.62	150.55	0.62	13.16	2251
Atricure	ATRC	32.10	31.19	-2.83	71.00	566
Atrion	ATRI	636.00	637.15	0.18	1.04	34
Avanos Medical	AVNS	57.15	62.74	9.78	35.86	2869
Axogen	AXGN	38.45	38.45	0.00	35.87	1529
Baxter Intl	BAX	72.35	71.50	-1.17	10.61	12034
Becton Dickinson	BDX	247.12	249.33	0.89	16.48	3996
Biolife Solutions	BLFS	18.67	19.72	5.62	228.67	1338
Bio-Rad Labs	BIO	312.18	319.80	2.44	33.99	716
Bio-Techne	TECH	166.34	178.68	7.42	37.92	1259
Biotelemetry	BEAT	55.15	56.95	3.26	90.47	1211
Boston Scientific	BSX	33.53	33.55	0.06	35.34	26751
Bovie Medical	BVX	4.94	4.83	-2.23	85.77	674
Bruker	BRKR	35.01	33.91	-3.14	-1.19	3021
Cancer Genetics	CGIX	0.92	0.95	3.26	-48.65	273
Cantel Medical	CMD	94.01	95.64	1.73	-7.03	798
Cardinal Health	CAH	50.30	48.40	-3.78	-21.01	15727
Cardiovascular Sys	CSII	37.02	37.64	1.67	58.89	1061
Caredx	CDNA	14.26	16.99	19.14	131.47	2059
CAS Medical Sys	CASM	2.21	2.67	20.81	246.75	2102
Celcuity	CELC	25.37	25.01	-1.42	31.98	40
Cellectar Biosci	CLRB	3.22	2.85	-11.49	-79.20	509
Cerus	CERS	7.03	7.16	1.85	111.83	2903
Check Cap	CHEK	3.27	3.22	-1.53	-69.16	187
Chembio Dx	CEMI	11.45	11.45	0.00	39.63	172
CHF Solutions	CHFS	1.68	1.02	-39.29	-70.52	2123
Conformis	CFMS	1.00	0.97	-3.00	-59.24	1621
Conmed	CNMD	80.08	76.42	-4.57	49.93	473
Cooper Companies	COO	260.31	253.26	-2.71	16.24	1188
Corindus Vascular	CVRS	1.05	0.92	-12.38	-8.91	5465
CRH Medical	CRHM	3.48	3.50	0.57	32.08	347
Cryolife	CRY	29.85	32.85	10.05	71.54	1079
Cutera	CUTR	39.60	34.60	-12.63	-23.70	2425
Cytosorbents	CTSO	11.63	11.55	-0.69	77.69	917
Danaher	DHR	101.37	100.33	-1.03	8.09	6571
Dariohealth	DRIO	1.23	1.22	-0.81	-23.85	160
Daxor	DXR	5.82	5.33	-8.42	16.56	17
Dentsply Intl	XRAY	47.73	39.02	-18.25	-40.73	35877
Dexcom	DXCM	123.33	123.35	0.02	114.93	4078
Digirad	DRAD	1.75	1.85	5.71	-28.16	307
Dynatronics	DYNT	2.85	2.86	0.35	-0.83	1
Edap Tms	EDAP	3.18	3.14	-1.26	9.41	100
Edwards Lifesci	EW	145.21	138.06	-4.92	22.49	4487
Ekso Bionics	EKSO	1.79	2.63	46.93	23.47	18544
Electrocore	ECOR	13.46	13.16	-2.23	-33.70	172
Electromed	ELMD	5.27	5.08	-3.61	-16.31	23
Endologix	ELGX	4.98	2.99	-39.96	-44.11	4743
Enzo Biochem	ENZ	4.48	4.14	-7.59	-49.20	508
Evolus	EOLS	20.13	20.76	3.13	80.52	1519
Fluidigm	FLDM	6.72	7.17	6.70	21.73	461
Fonar	FONR	26.75	26.85	0.37	10.27	56
Fresenius Medical	FMS	49.99	47.90	-4.18	-8.85	439
Genmark Dx	GNMK	7.31	7.38	0.96	76.98	553
Genomic Health	GHDX	54.28	54.25	-0.06	58.63	1074
Glaukos Corp	GKOS	39.39	41.95	6.50	63.55	1153
Globus Medical	GMED	52.69	52.35	-0.65	27.37	2371
Grifols	GRFS	21.52	20.92	-2.79	-8.73	3952
Haemonetics	HAE	96.71	99.74	3.13	71.73	3361
Henry Schein	HSIC	80.23	77.37	-3.56	10.72	5217
Hill-Rom	HRC	94.38	95.00	0.66	12.71	2061
Hologic	HOLX	42.11	40.66	-3.44	-4.89	6225
HTG Molecular Dx	HTGM	2.80	3.58	27.86	76.35	4184
Icad	ICAD	2.93	2.90	-1.02	-15.70	287
ICU Medical	ICUI	293.35	292.40	-0.32	35.37	1208
Illumina	ILMN	332.49	330.25	-0.67	51.15	3530
Inogen	INGN	211.53	227.09	7.36	90.70	1757
Inovio Pharma	INO	3.94	4.46	13.20	7.99	4422
Inspire	INSP	46.46	46.33	-0.28	85.47	994
Insulet	PODD	85.89	87.02	1.32	26.12	2230
Integer	ITGR	70.75	70.70	-0.07	56.07	828
Integra Lifesci	IART	63.37	62.88	-0.77	31.38	3118
Interpace Dx	IDXG	1.00	1.07	7.00	4.90	1925
Intersect ENT	XENT	26.40	27.50	4.17	-15.12	1418
Intricon	IIN	64.00	65.55	2.42	231.06	853
Intuitive Surgical	ISRG	522.60	521.02	-0.30	42.77	1563
Invacare	IVC	18.00	16.75	-6.94	-0.59	2173
Invitae	NVTA	8.26	9.95	20.46	9.58	9559
Invivo Therapeut	NVIV	1.98	1.98	0.00	-89.71	521
Invuity	IVTY	3.90	3.60	-7.69	-41.94	228
Iradimed	IRMD	25.15	27.70	10.14	82.84	646
Irhythm	IRTC	84.50	83.89	-0.72	49.67	859
Iridex	IRIX	7.60	8.00	5.26	4.99	57
K2M Group	KTWO	21.77	20.85	-4.23	15.83	788
Labcorp	LH	178.91	179.59	0.38	12.59	2292
Lantheus Holdings	LNTH	13.60	13.10	-3.68	-35.94	818
Lemaitre Vascular	LMAT	35.54	36.58	2.93	14.89	365
Lianluo Smart	LLIT	1.85	1.88	1.62	7.43	25
Livanova	LIVN	121.49	122.98	1.23	53.88	1011
Luminex	LMNX	34.60	27.20	-21.39	38.07	4373
Masimo	MASI	108.26	109.63	1.27	29.28	1530
Mazor Robotics	MZOR	53.18	49.72	-6.51	-3.64	3011
Medigus	MDGS	3.19	3.04	-4.70	-42.42	189
Medtronic	MDT	90.48	90.60	0.13	12.20	15496
Meridian Biosci	VIVO	15.35	15.00	-2.28	7.14	494
Merit Medical Sys	MMSI	55.75	54.75	-1.79	26.74	1295
Mesa Labs	MLAB	193.94	203.30	4.83	63.56	97
Microbot Medical	MBOT	0.61	0.63	3.28	-38.24	1969
Micron Solutions	MICR	3.14	3.30	5.10	-5.71	62
Milestone Scientific	MLSS	0.84	0.83	-1.19	-29.66	12
Mimedx Group	MDXG	4.16	4.29	3.13	-65.98	5475
Misonix	MSON	17.10	17.50	2.34	85.19	79
Motus GI	MOTS	6.17	5.99	-2.92	36.76	221
Myomo	MYO	2.29	2.06	-10.04	-45.07	1242
Nanostring Tech	NSTG	12.34	14.00	13.45	87.42	1113
Natera	NTRA	23.64	25.22	6.68	180.53	2712
Natus Medical	BABY	36.40	35.50	-2.47	-7.07	710
Neurometrix	NURO	1.21	1.21	0.00	-30.02	93
Neuronetics	STIM	24.60	33.51	36.22	20.63	222
Nevro	NVRO	58.94	64.23	8.98	-6.97	1919
Novocure	NVCR	34.75	35.95	3.45	77.97	1233
Nuvasive	NUVA	63.92	64.56	1.00	10.38	1643
Nuvectra	NVTR	15.41	18.14	17.72	133.76	1050
Nxstage Medical	NXTM	28.08	28.30	0.78	16.80	1309
Obalon Therapeutics	OBLN	1.63	1.76	7.98	-73.37	297

Continues on next page

BioWorld MedTech stock report for public med-tech companies

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Company	Symbol	Close 8/3	Close 8/10	Change Week	Change YTD	Vol (000)
Oncocyte	OCX	2.30	2.60	13.04	-44.09	253
Opko Health	OPK	5.89	5.42	-7.98	10.61	23424
Optinose	OPTN	21.38	20.98	-1.87	11.01	649
Orasure Tech	OSUR	16.80	16.76	-0.24	-11.13	2576
Orthofix Intl	OFIX	61.27	53.96	-11.93	-1.35	1444
Orthopediatrics	KIDS	27.53	27.59	0.22	43.77	304
Oxford Immunotec	OXFD	14.33	14.47	0.98	3.58	200
Pacific Biosci	PACB	3.81	4.40	15.49	66.67	5857
Pavmed	PAVM	1.49	1.44	-3.36	-36.99	1290
Penumbra	PEN	146.05	124.35	-14.86	32.15	3445
Perkinelmer	PKI	86.32	84.92	-1.62	16.14	1696
Precision Therapeu	AIPT	1.21	1.26	4.13	24.75	457
Presbia	LENS	2.06	2.13	3.40	-43.65	104
Pro-Dex	PDEX	6.20	6.72	8.39	-1.18	52
Pulse Biosci	PLSE	12.83	15.03	17.15	-36.31	184
Quest Dx	DGX	108.84	108.53	-0.28	10.19	2976
Quidel	QDEL	70.87	69.7	-1.65	60.78	2549
Quotient	QTNT	7.60	7.71	1.45	55.76	1070
Radnet	RDNT	14.00	14.05	0.36	39.11	765
Reshape Lifesci	RSLS	0.45	0.10	-77.78	-93.24	87267
Resmed	RMD	104.74	107.78	2.90	27.26	2973
Restoration Robotics	HAIR	2.83	1.48	-47.70	-67.83	4502
Retractable Tech	RVP	0.77	0.77	0.00	13.24	243
Rewalk Robotics	RWLK	0.82	0.95	15.85	-13.64	2800
Royal Philips NV	PHG	43.82	42.91	-2.08	13.52	2730
RTI Surgical	RTIX	4.60	4.50	-2.17	-79.73	312
Seaspine	SPNE	13.79	13.90	0.80	37.35	164
Second Sight	EYES	1.66	1.61	-3.01	-15.71	1139
Senseonics	SENS	3.92	4.08	4.08	53.38	6514
Sensus Healthcare	SRTS	7.10	7.14	0.56	38.37	138
Sientra	SIEN	20.77	20.89	0.58	48.58	1856
Smith & Nephew	SNN	35.94	35.20	-2.06	0.54	1099
Staar Surgical	STAA	37.90	39.95	5.41	157.74	3060
Steris	STE	116.75	114.83	-1.64	31.28	2465
Strata Skin Sci	SSKN	2.06	2.08	0.97	69.11	585
Stryker	SYK	165.30	165.88	0.35	7.13	3595
Surmodics	SRDX	59.35	70.45	18.70	151.61	711
T2 Biosystems	TTOO	5.36	6.47	20.71	57.04	2709
Tactile Systems	TCMD	50.84	57.15	12.41	97.20	1557
Tandem Diabetes	TNDM	33.03	30.90	-6.45	1209.32	9802
Teladoc	TDOC	62.50	71.85	14.96	106.17	8528
Teleflex	TFX	245.86	228.13	-7.21	-8.32	1166
Thermo Fisher Sci	TMO	233.32	231.42	-0.81	21.88	3670
Transenterix	TRXC	5.23	4.76	-8.99	146.63	28451
Trinity Biotech	TRIB	4.63	4.49	-3.02	-11.96	96
Utah Medical	UTMD	96.45	91.10	-5.55	11.92	59
Valeritas	VLRX	1.49	1.51	1.34	-47.02	1588
Varian Medical Sys	VAR	114.77	111.18	-3.13	0.03	2304
Veracyte	VCYT	11.16	12.00	7.53	83.77	1400
Vericel	VCEL	10.15	12.90	27.09	136.70	6757
Vermillion	VRML	0.63	0.55	-12.70	-71.50	460
Viewray	VRAY	11.05	9.89	-10.50	6.80	6743
Viveve Medical	VIVE	2.58	2.60	0.78	-47.69	603
Vocera Comm	VCRA	30.90	31.32	1.36	3.64	564
Volitionrx	VNRX	1.73	1.69	-2.31	-42.52	477
West Pharma	WST	114.75	114.82	0.06	16.37	1107
Wright Medical	WMGI	26.01	28.07	7.92	26.44	8518
Xtant Medical	XTNT	5.80	6.05	4.31	-11.94	28
Zimmer Biomet	ZBH	125.91	122.57	-2.65	1.57	2635

Notes

Trading volumes for Nasdaq, Amex and NYSE are recorded as the total number of shares traded (in thousands) on a weekly basis (cumulative Monday through Friday); the weekly and YTD changes are from IPO completion, where applicable.

Average percent change week: +0.46%
Range: -77.78% to +46.93%; Number of companies: 187 (not market weighted)

Average percent change year-to-date: +27.10%
Range: -93.24% to +1,209.32%; Number of companies: 187 (not market weighted)

10 biggest U.S. gainers for the week

Share price by percent		Share price by dollars	
Ekso Bionics	46.93	Inogen	15.56
Neuronetics	36.22	Bio-Techne	12.34
HTG Molecular Dx	27.86	Surmodics	11.10
Vericel	27.09	Mesa Labs	9.36
CAS Medical Sys	20.81	Teladoc	9.35
T2 Biosystems	20.71	Neuronetics	8.91
Invitae	20.46	Bio-Rad Labs	7.62
Caredx	19.14	Tactile Systems	6.31
Surmodics	18.70	Avanos Medical	5.59
Nuvectra	17.72	Nevro	5.29

10 biggest U.S. losers for the week

Share price by percent		Share price by dollars	
Endologix	-39.96	Penumbra	-21.70
Luminex	-21.39	Teleflex	-17.73
Dentsply Intl	-18.25	Dentsply Intl	-8.71
Penumbra	-14.86	Luminex	-7.40
Cutera	-12.63	Orthofix Intl	-7.31
Orthofix Intl	-11.93	Edwards Lifesci	-7.15
Cellectar Biosci	-11.49	Cooper Companies	-7.05
Viewray	-10.50	Utah Medical	-5.35
Myomo	-10.04	Cutera	-5.00
Apollo Endosurgery	-9.47	Conmed	-3.66

Nuvasive

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Diego-based Nuvasive with the Cios Spin mobile imaging tool from Erlangen, Germany-based Siemens Healthineers, which is used for intraoperative quality assurance. The partners will co-develop and co-market the result in the U.S., with the potential to expand into other markets.

Better together

"Using the two systems together – the Siemens' Cios Spin and the Nuvasive Pulse platform – will provide an integrated solution that can offer workflow improvement to a surgeon at a more economical price point to the hospital," Matt Link, Nuvasive EVP of strategy, technology and corporate development explained to *BioWorld MedTech*.

"For example, the smaller footprint is more manageable than a CT scan in a crowded OR," he added. This combined solution will be procedurally integrated specifically with the surgeon's workflow in mind to drive higher utilization."

The expectation is that the integrated system will provide improved anatomical visualization during surgery, which is expected to improve surgical anatomical access and spinal implant placement. The partners plan to highlight their approach at the North American Spine Society 2018 Annual Meeting coming up Sept. 26 to Sept. 29, 2018, in Los Angeles.

Nuvasive recently gained FDA clearance for the Pulse system, which is the first integrated spine surgery automation platform. (See *BioWorld MedTech*, July 30, 2018.) Wall Street seems to be embracing the deal, sending Nuvasive shares (NASDAQ:NUVA) up 2 percent since it was reported on Aug. 9.

"The partnership allows Nuvasive to: (1) add next-generation imaging to its platform, (2) drive capital sales and (3) ultimately increase implant pull through. The partnership with a big box company was a next step that we had anticipated, and with an installed base of 20k systems globally, we believe Siemens could prove to be a good partner for Nuvasive," summed up Wells Fargo analyst Larry Biegelsen in a note. "We would expect the relationship to evolve over time as Siemens upgrades its U.S. installed base to the new imaging system that is pending FDA approval.

Capabilities combined

Pulse already brings together 2D and 3D navigation, smart imaging capabilities, as well as neuromonitoring, surgical planning, radiation reduction and patient-specific rod bending technologies.

It's designed to upgrade and replace what's often an operating room filled with imaging and monitoring equipment from various vendors. The expectation is that the Pulse system offers one stop for integrated presurgical planning, OR guidance and outcomes review for any spinal procedure. Nuvasive defines this as 'Surgical Intelligence.'

Currently, many hospitals and health care systems treat patients undergoing spine surgery through often cost-intensive, intraoperative CT scans with a general navigation system that has limited usefulness in spine surgery cases.

"Minimally invasive spine (MIS) surgery has many advantages for the patient, including minimized tissue disruption, blood loss, rates of infection and thus, faster recovery. These advantages, however, are frequently offset by new challenges inherent to MIS, including reduced visualization, higher radiation exposure, screw placement accuracy, alignment correction and neural integrity," said Link.

"Though some solutions exist for each of these challenges, surgeons are presented in the OR with disparate technologies that often require dedicated people resources to operate. The Pulse platform is designed to address these challenges by providing a cost-effective, singular source of information for surgical teams," he concluded.

For Siemens, this is an opportunity to integrate its imaging technology into a novel technology approach that could advance spine surgery outcomes. "We at Siemens Healthineers are excited to work with Nuvasive to develop intraoperative 3D-imaging and navigation tools for our advanced imaging systems that empower spine surgeons and neurosurgeons to be more precise, faster and cost efficient in the operating room," said Peter Seitz, head of surgery at Siemens Healthineers. "Increased workflow efficiency, better image quality, as well as predictable and reproducible results, will transform care delivery and set a new standard in spine surgery." ♦

China

Continued from page 1

which will end up making the commercialization of devices faster.

As an effort to standardize classification and streamline the registration process, the draft last year represented the first amendment in 15 years since the classification catalog was released in 2002.

"As regulatory control of medical devices in China hinges on classification, the changes imposed by the new catalogue will have considerable impact on medical device registration, manufacturing and distribution," Qian Zhou, senior associate of legal research & publications at management consulting firm Dezan Shira & Associates, told *BioWorld MedTech*.

Zhou said the new catalog has made it easier for companies to categorize new devices. They can easily register their medical devices at a lower cost as well.

More systematic classification

Compared to the 2012 edition, the new catalog reduces the number of device categories from 43 to 22. Medical devices are divided into the 22 categories according to their technical specialty and clinical use characteristics.

The new catalog also reclassifies the previous 260 device types into 206 primary types, and further divides them into 1,157 secondary types.

For example, magnetic resonance imaging machine under the imaging device category is divided into three secondary types, namely closed bore, open bore, and dipolar electromagnet configuration.

Furthermore, to each secondary type, the new catalog adds detailed descriptions of the features and the intended uses of the devices, with 6,609 product name examples.

"The classification of medical devices becomes more scientific and instructive. All of these changes will offer far more certainty as to which category a given product falls under," Zhou noted.

Such detailed information added to each secondary type helps determine the management class of the devices, which are organized as class I, II or III devices based on the risk level they present to patients or users from low to high.

For instance, hooks used in orthopedic surgeries that carry low risks are class I devices, but a magnetic resonance imaging machine is a class III device because it poses high risks.

Easier registration

The overhaul this time also downgraded the management class of 40 types of devices that come with a longer marketing period, a higher maturity level and controllable risks.

Chunqing Zhang, senior engineer at the Medical Device Standards Management Center of the CNDA, cited a few examples at a press conference held by the CNDA.

"Infusion pumps for radiofrequency ablation devices are moved from class III to class II. Meanwhile, class II devices such as light-emitting diode surgery lighting and microplate washers are lowered to class I," said Zhang.

> *"As regulatory control of medical devices in China hinges on classification, the changes imposed by the new catalogue will have considerable impact on medical device registration, manufacturing and distribution.*
>
> Qian Zhou
> Dezan Shira & Associates

Under the current system, different classes require registration with authorities at different levels. In other words, companies may get registration done locally for devices now for devices of a lower management class.

Being lower class a good thing

Such a transfer to a lower management class means registration can be done much faster and cheaper.

"For medical devices moved from class III to class II, the companies can register these devices to the provincial level regulators, rather than the CNDA in Beijing," said Zhou.

"For those moved from class II to class I, they can save the troublesome registration process. As an alternative, they can just make a much simpler record-filing with the local regulators," Zhou added.

According to consultancy firm Emergo Group, marketing approval could come in less than a week for class I devices, and 12 to 20 months for class II devices, compared to up to 22 months for class III devices. The overall cost of gaining the approval is also lower for class I devices.

"For medical devices being moved to lower classes, the companies should make renewal application or record-filing with the corresponding regulators six months prior to the expiry of their old certificate," Zhou advised.

At the same time, several devices were transferred to higher management classes.

"For certain medical devices being moved from class II to class III, the registration process actually turns to be stricter. Going forward, the follow-up supervision is expected to be stricter as well," said Zhou.

Currently, registrations for class II and III devices in China require in-country testing and clinical trial data.

Zhou added that for medical devices being regarded as riskier and raised to higher classes, manufacturers should make a new registration before Aug. 31, 2019.

Part of the regulatory reform

A 15-year gap in updating the classification catalog means the overhaul is much needed.

"The original catalog can no longer keep up with the rapid development of the medical device industry," said Zhexiong

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Australia

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players may not have had an opportunity to engage with the TGA, or may not have a full understanding of Australia's regulatory requirements.

Challenges in the CSfMD space are increasing, and the complexity of the cyber threat landscape and lack of regulatory guidelines require immediate attention, the agency said.

To gather information, the TGA has engaged The Commonwealth Scientific and Industrial Research Organization (CSIRO) – an independent Australian federal government agency responsible for scientific research – to conduct research to better understand the innovators in the SaMD space, and how the TGA can support them in demonstrating safety of their products.

CSIRO is reaching out to the emerging cluster of technology developers that are focused on producing health and medical software, including clinical decision support tools and companion apps for devices.

SaMD is a bit of a gray area in Australia, Arthur Brandwood, founder and principal consultant at Brandwood Biomedical, told *BioWorld MedTech*.

He clarified that the TGA is not developing its own guidance in this area. The agency circulated guidance from the International Medical Device Regulators Forum (IMDRF) last year and is proposing to adopt IMDRF guidance in Australia.

Historically, Australia tends to follow EU regulations in the device space, and medical device software used for therapeutic purposes is regulated under the medical devices regulatory framework. Mobile apps would be considered within this framework.

According to IMDRF principles, the TGA would classify software as a medical device when it is intended for diagnosis, prevention, monitoring or treatment or alleviation of disease as compared to software that measures well-being.

For example, software that analyzes clinical data, such as the results of blood tests would be considered a medical device. In addition, software used in manufacturing and for maintaining a quality management system is also regulated.

However, not all medical software is regulated by the TGA. Exclusions to regulation would include software that is used for information purposes or as advice to health professionals.

Regulation is risk-based, and what matters is the intended use of the software and what the manufacturer puts on the label, Brandwood said. The TGA has an information line, and manufacturers can request a preconsultation on classification.

Manufacturers of medical device software products (aside from lower-risk class I products) need to obtain conformity assessment certification, and all devices are expected to meet essential principles for safety and performance, Brandwood said.

One of the biggest areas of concern for SaMD is the reporting of post-market incidents and complaints, because many software issues are managed as a "reboot," and often users don't identify issues. Similarly, software issues are often misidentified as "user issues," Brandwood said.

Cybersecurity threats

CSIRO will be conducting research into medical device cybersecurity to support a guidance document to help the device ecosystem implement best practices approaches to cybersecurity.

To that end, it will be holding a national workshop and webinar on Sept. 14 in Canberra to engage with developers, sponsors and users of medical devices. The focus of the workshop is to explore and capture the complexities of the Australian medical device cybersecurity landscape before developing a new guidance.

Although there have been no reports of hacking attacks on medical devices in Australia, there have been reports of such attacks overseas, the TGA said, and cybersecurity experts in Australia have demonstrated a wide range of potential vulnerabilities in simulated attacks.

These experts have identified a wide range of medical devices as potentially vulnerable to unwanted intrusion, including technology as diverse as PET scanners, infusion pumps and life-support equipment.

Devices incorporating wireless communications are particularly vulnerable as potential hackers can operate them remotely. Common medical devices that use wireless communications include: infusion pumps, insulin pumps, implantable drug pumps, implantable cardiac defibrillators, pacemakers, neural stimulators, insulin pumps, telemetry heart monitors and infant/fetal monitors.

The TGA advises device manufacturers to perform risk assessments by examining the specific clinical use of potentially affected products in the host environment. An IT risk assessment should include:

- The access control list – a list of accounts and passwords and policies and how they are accessible (remote/physical). Are there hard-coded (backdoor) passwords that never change? Are passwords stored as plain text or encrypted? Are there documented access levels and identities associated with each level?
- Physical access – is access to advanced features gained through a password or keypad? Is remote access to advanced features available?
- Data validation – can anyone write to memory?
- Remote access – is there a wireless card?
- Log files – are data events recorded in a file with adequate detail for later assessment (who, what, when, how)?
- Ports and services – what ports and services are used? What is the default state of unused services and ports? Can unused ports/services be disabled?
- Malware protection – is anti-virus software allowed/installed?
- Wireless and/or wired – what are the default settings? What protocol is used? How are keys managed?
- Backup – can configuration, software settings and logs be backed up and restored?
- Checksum – is there boot-up or run-time checksums used to detect changes to software? ♦

IVDs

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things would provide considerable regulatory discretion for tests from pre-certified labs.

The FDA released a discussion draft in January 2017 that gave an overview of a potential regulatory framework for lab-developed tests (LDTs), but the question largely slipped out of public view as 2017 unwound. The question arose again at the 2018 annual meeting of the American Clinical Laboratory Association (ACLA), however, during which FDA commissioner Scott Gottlieb said he saw a need for comprehensive legislation. Gottlieb also noted that the agency's staff was at the time already working on materials that could be used in drafting legislative language. (See *BioWorld MedTech*, March 7, 2018.)

The most recent legislation addressing the matter is the Diagnostic Accuracy and Innovation Act (DAIA) of 2017, sponsored by Reps. Diana DeGette (D-Colo.) and Larry Bucshon (R-Ind.), although that legislation languished pending the FDA's feedback on the question. DAIA would have provided a new FDA center exclusively for IVDs, and a summary said that the 510(k) process would not be pertinent to IVDs. The legislation also provided for a novel premarket review process for high- and moderate-risk tests, and the associated user fees would reflect those required for PMA and 510(k) filings.

This legislation and the FDA's effort to provide technical assistance were the subjects of a stakeholder letter to four members of the House and Senate, which expressed the hope that "comprehensive diagnostics regulatory reform is enacted in 2018." Among the signers of the letter are AdvaMed Dx and the Biotechnology Innovation Organization, but the ACLA is also on board. The Aug. 8 letter said that the signers were still examining the FDA technical assistance (TA) document, which they characterized as "an important and necessary next step in the pursuit of comprehensive legislative reform."

The FDA's overview of the TA document said that the agency is of the view that "an optional pre-certification program" may prove less cumbersome for development of IVDs, which are referred to as in vitro clinical tests (IVCTs). The overview document stated further that the pre-cert process – which would bear at least some resemblance to the still-developing pre-cert program for digital health – would call for organizational re-certification at two years, but this new paradigm would provide "appropriate mechanisms" for grandfathering tests that are already on the market. The pre-cert notion is in use for DTC tests that determine the customer's genetic health risk as well.

The full TA document notes that anyone who has committed a "significant violation" of the relevant portions of the statute in the prior five years would not be eligible for the IVCT pre-cert program. A first-of-a-kind IVCT would also not be eligible, nor would be any tests used in tissue donation/collection.

For-cause inspections included in TA

A pre-certification would be granted upon the applicant's demonstration that their processes provide a reasonable assurance of analytical and clinical validity, but the TA also said that the applicant would have to demonstrate also that it employs methods and its facilities "conform to the requirements of section [quality systems]." The document further suggests the FDA would prefer to retain the right to conduct a for-cause inspection as demonstrated by the passage stating that the applicant would allow an FDA employee to examine any and all records pertaining to possible adulteration or misbranding.

Most labs would be subject to only a subset of the Quality Systems Regulations, such as design controls, purchasing controls, and corrective and preventive action, although the agency said that labs dealing with tissues would be subject to a more exhaustive subset of the QSRs. This would include statistical trending and management review. Generally speaking, high-risk tests would not be exempt from any of the existing regulatory requirements, and thus would not be eligible for the pre-cert program, and tests that are conducted fewer than 8,000 times a year would be exempt only from premarket review. The volume ceiling of 8,000 per year is the same as the maximum volume for the humanitarian device exemption, a figure that was doubled by the 21st Century Cures Act.

Also exempt are tests for law enforcement and public health surveillance uses, but investigational tests would likewise be exempt. It does not appear that this last exemption would apply to IVDs used in clinical investigations of therapeutic products, the subject of a December 2017 draft guidance that drew substantial criticism from stakeholders. (See *BioWorld MedTech*, April 3, 2018.)

A change to one or more tests that fall under a pre-certification order could be made immediately and reported to the agency within 30 days if such a change were necessary to address a potential risk to public health. Such a change would be limited to a "new specification or test method" invoked to address that consideration, although this provision generally seems to reflect the CBE-30 mechanism already in use at more than one center at the FDA.

Not so fast on new center

Khatereh Calleja, senior VP for technology and regulatory affairs at the Advanced Medical Technology Association, told *BioWorld MedTech* that there is at least one critical difference between DAIA and the FDA document. "A new center is not called out" in the FDA approach, Calleja said, but she said that IVCTs may nonetheless be handled separately under the agency's approach. "The anticipation is [IVCTs] would have their own organization, just not necessarily in a new center," she said, although she noted that the Office of In Vitro Diagnostics and Radiological Health (OIVR) is already equipped for in vitro diagnostic regulation. Calleja said it is not clear whether the agency would be inclined to organizationally separate the two functional domains of OIVR.

Calleja said there is also a considerable degree of uncertainty as to how the 510(k) and PMA programs might be adjusted

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Coaptech

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the company recently passed the two-year mark, but he met Steven Tropello, who serves as founder and CMO, while they were at Johns Hopkins.

The technology came about as a result of an event experienced by Tropello. "I'm an emergency critical care physician," he told *BioWorld MedTech*. "I was working an emergency shift – almost five years ago now – at an inner-city Baltimore site." One day, a patient arrived, having pulled out her permanent feeding tube, a situation that posed a problem for Tropello.

"She'd had a stroke and couldn't feed herself. Emergency physicians will try to place [feeding tubes] in, if they can, blindly, but I wasn't able to do it, due to anatomy," Tropello said. He had hoped the on-call gastroenterologist would be able to redo the procedure, but was met with pushback. The person on-call had too much to do and could not perform the procedure until the next day.

"That response is very similar to other indolent and delayed mindsets we often see in medicine, and I just got frustrated." He knew the procedure was not very difficult compared with other interventions he performed, but he did not have training on an endoscope. "What can I do to try to make this procedure tangible to a guy like me," he asked himself. Although ultrasound machines are ubiquitous today, that was not the case 10 years ago. In fact, there was only one ultrasound machine in his department. The incident prompted him to go home and think, and it was then that he first visualized the Coaptive Ultrasound technology.

Safety, ease of use

"It's not rocket science; it's pretty straightforward. You take magnetized internal catheters and place them into the body cavities [in which] you want to do the procedure," Tropello explained. These catheters are controllable by an external magnet and visualized under ultrasound. The two magnets try to pull each other together, and the physician, via ultrasound, can determine how to place the feeding tube safely.

Carolan noted that ultrasound has transformed medicine, "but it does not do a great job in hollow organs," such as the stomach or lungs. "This invention allows ultrasound to be used safely and effectively in hollow organs. There's a ton of different directions you can go with this," Carolan said of the PUMA platform.

The technology allows for the simulation of fluid-filled organs. Balloons, which are filled with fluid, are placed into a hollow organ, and the magnets "squish" the tissue together. It effectively makes the balloon part of the tissue, permitting ultrasound. The novel procedure is known as percutaneous ultrasound gastrostomy (PUG).

With the technology, the use of endoscopes for gastrostomy tube placement could be cut down. As Carolan noted, endoscopes often require the transfer of a patient to the surgical suite. Further, they are reusable, posing a risk for cross-contamination. Another way to perform the procedure involves fluoroscopy, which involves ionizing radiation. This poses a cancer risk to some patients. Both approaches also involve risk, additional costs and delay. The company has estimated a 33 percent to 50 percent reduction in procedure time.

With this system, hospitals can use the ultrasound machines they already have in place. They can save time, effort and money, Carolan said.

While the procedure could change how feeding tubes are placed, the company sees other potential avenues for the technology in additional organs.

"Things are moving very quickly," Carolan said, adding that the company has conducted good laboratory practice canine studies, allowing them to rev up the strength of magnets. The dogs were unharmed and recovered. The company is building out its technical file and clearance could come as early as next year.

Coaptech has the backing of funders, particularly local angels, as well as NIH and Maryland tech programs, such as the Maryland Technology Development Corp., the Maryland Industrial Partnerships program and UM Ventures, a joint initiative of the University of Maryland, Baltimore and University of Maryland, College Park. Ahead of commercialization, the company aims to bring in $7 million to $10 million.

Carolan noted that the platform could extend into other procedures. In addition, the company has a robust R&D pipeline with other PUMA devices currently being prototyped. ♦

Cancer

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analysis of multiple cell lines in use at laboratories around the world.

As the most striking example of the consequences of that diversity, when 27 strains of the estrogen receptor-positive breast cancer cell line MCF7 were tested against 321 cancer drugs, at least 75 percent of those that strongly inhibited some strains were inactive against others.

The genetic changes were associated with differential gene expression and marked differences in cell morphology and proliferation.

"We've known for decades that cell lines evolve in culture and can start behaving in a weird way," said Uri Ben-David told *BioWorld MedTech*. "It's been like a dirty secret."

Ben-David is lead author of a paper mapping that diversity published online in *Nature* on Aug. 7, 2018.

In addition to testing multiple cancer cell lines, the researchers looked at three noncancer cell lines, finding genetic diversity in those, too. "They all exhibited the same phenomenon," Ben-David said. "In one cell line, the extent was the same as in cancer cell lines."

Taken together, the findings highlight the need for researchers to understand how the cells they are using have diverged genetically from their parent line.

Help is on the way

To help with that, Ben-David and colleagues at the Broad Institute of Harvard and MIT, are this week launching a website, Cell Strainer (https://cellstrainer.broadinstitute.org), where users can upload cell line genomic data and measure their strain's genetic distance from a reference in the Cancer Cell Line Encyclopedia (CCLE), which is held at the Broad.

"You can't prevent genetic diversification, but you can alleviate or control for it," said Ben-David.

The news is not all bad. The capacity for evolution and its consequences for drug activity could be used to track the development of drug resistance. "The strains still have the same genetic background – you can try to tease out the mechanism of action of a small molecule, or, with drugs with a known target, you could check it actually works [in the expected way]," Ben-David said.

The starting point for the extensive piece of research reported in *Nature* was a re-analysis of the sequencing data of 106 cancer cell lines held by two of the world's leading cell custodians, in the Broad Institute's CCLE and the Genomics of Drug Sensitivity in Cancer collection held by the Sanger Institute in Cambridge, U.K.

The 106 lines should be genetically identical, but there were high levels of variability. A median of 19 percent of non-silent mutations (range 10 percent to 90 percent) were found in only one of the two datasets. Similarly, 26 percent of genes that had copy number alterations were discordant.

The results indicate genetic variability across cultures of the same cell line is common. "We were surprised at how heterogeneous the cultures actually are," said Ben-David. The diversity in the 106 cancer cell lines may be the tip of an iceberg. "Both the Broad and the Sanger know how to work with cell lines, so this is probably an underestimate of the level of heterogeneity as a whole," he said.

The researchers next performed extensive genomic characterization of 27 strains of the MCF7 breast cancer cell line. Here, they detected 283 genes with copy number gains and 405 with copy number losses in one of the strains. Only a small majority of those changes – 13 percent of gains and 21 percent of losses – were detected in all the strains.

The differential events included genes that are commonly gained or lost in breast cancer, including TP53, PTEN, EGFR and Map2K4. PTEN, for example, was deleted in 17 strains and retained in 10.

Overall, it was estimated that 45 percent of all genetic variation was occurring at a subclonal level. The researchers subsequently demonstrated that was driven by changes in culture conditions. "Even a slight difference in culture conditions induces selection," Ben-David said.

Despite an overall similarity in their gene expression profiles, the 27 strains also showed extensive variation in their transcriptomes. In all, 654 genes were differentially expressed by at least twofold between pairs of strains.

To exclude the possibility that the variation across MCF7 strains was an artefact of that cell line, the researchers did the same analysis on 23 strains of the A549 cancer cell line, observing similar variation.

The significance of the variation is underlined by the fact that transcriptome analysis found KRAS signaling was the most variable pathway in A549, a cell line that is a commonly used model of KRAS-dependent cancer.

The findings were replicated in multiple strains of 11 other cell lines sourced from different labs. That analysis showed genetic instability is not limited to transformed cancer cell lines; variation across 15 strains of MCF10A, a non-transformed human mammary cell line, was as high as in MCF7 cancer cells.

Functional consequences

That the extensive genomic variation matters is highlighted by differences in cell properties such as doubling times, size and shape seen among strains.

The genomic instability of the MCF7 strains had a major effect on drug response. Of 321 drugs tested, 55 had strong activity against at least one of the 27 strains. However, at least one strain was entirely resistant to 48 of those 55 compounds.

Drug response was associated with transcriptional differences in relevant pathways. For example, strains sensitive to CDK inhibitors had an up-regulated cell cycle signature. Meanwhile, strains sensitive to PI3K inhibitors had an up-regulated mTOR signature.

Of note, the strains that were the most resistant to drugs in general had down-regulated drug metabolism pathways.

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China

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Wang, officer at the Department of Medical Device Registration of the CNDA.

"There was overlapping among the categories and missing key information such as product description and intended uses. The original catalog also failed to cover new products and new device types," said Wang.

Classifying a device is just the first step to tap into the Chinese market. To bring devices to the Chinese patients faster, the CNDA has rolled out other measures to streamline its regulatory system.

This year, the CNDA drafted the amendment that allows the medical device developers to seek contract manufacturers, relaxes the requirements for clinical evaluation for class I devices and waives the need to provide a certificate that shows the marketing approval from the home country of a device that is yet to be launched in China. (See *BioWorld MedTech*, Jun. 28, 2018.) ♦

IVDs

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or supplanted entirely. "The current reform elements have all aimed at a risk-based framework," she said, adding that a substantial volume of information is at the ready for test evaluation, such as clinical practice guidelines and the diagnostic literature. "I think the idea to leverage what we know" is effective to provide risk mitigation, such as special controls, she said.

Susan Van Meter, the executive director of AdvaMed Dx, said the digital health pre-cert program cannot be simply copied and pasted for use in this in vitro program. "I think there are some similarities in the approach," Van Meter said, adding, "we can look to some principles that are there, but this is a different construct." She said the FDA document provides a highly useful basis for formation of such a program, noting, "we think pre-cert could be tremendously beneficial to ensure innovations are made quickly available to patients." ♦

Cancer

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Broadly speaking, clustering of MCF7 strains based on their drug response was highly similar to clustering based on genetics or gene expression, leading the researchers to suggest that as a route to uncovering mechanisms of drug sensitivity and resistance.

Having exposed the extent of variation, the researchers suggest their Cell Strainer database is the best way to understand and control for it.

Ben-David said researchers could then self-certify that their cell lines have not changed significantly from the reference point when submitting journal papers.

There are precedents in an existing requirement to check for mycoplasma contamination of cell lines, and authentication standards introduced in 2010 to prevent mislabeling or misidentification of cell lines.

"If you want to publish data that make comparisons with other research, you would need to check the box 'my cell lines have not diverged,'" said Ben-David.

That also will increase understanding of cell line divergence across the world. "Now we understand how it affects gene expression and drug response, you can learn a lot from divergence," Ben-David said. "This is not just a cautionary tale, it opens the way to interesting biology." ♦

Product briefs

Researchers at **Okayama University** reported in *The Journal of Vascular Access* a supporting device for accurately placing hemodialysis catheters on kidney patients. The device was successfully used on a group of 10 Japanese adult hemodialysis patients and is expected to become an essential tool in situations where other, catheter-free hemodialysis approaches are not possible. The researchers' insertion support device accommodates for individual body shape differences and is expected to decrease the rate of tunneled cuffed catheter (TCC) replacements – typically ranging between 8.9 percent and 56 percent. The device is made from a material called expanded polytetrafluoroethylene, having the property of maintained plasticity. It can be described as a bendable ribbon with eyelets spaced 1 cm apart; the holes allow making markings on the patient's body with a felt-tip pen. Placement of the device on the body took place with the help of X-ray imaging: the tip of the device, for marking the TCC entry site, was laid so that it overlaps with the right heart border. With the help of the markings made on the patient's body, the physician could insert the TCC within an error of about 1 cm. The patients were observed for two months, during which there was no catheter replacement needed. The article, "New insertion support device assisted the accurate placement of tunnelled cuffed catheter: first experience of 10 cases," was first published May 1, 2018.

Neurology Extra

Keeping you up to date on recent developments in neurology

By Andrea Applegate, Production Editor

Skills and learning improved by closed-loop electrical brain stimulation during sleep

Malibu, Caif.-based Hrl Laboratories LLC, in collaboration with University of New Mexico, have published the first study showing that transcranial alternating current stimulation (tACS) of the brain during sleep increases human subjects' ability to accurately assess hidden targets in novel visual scenes. The new "closed-loop" method effectively reduces the typical overnight drop in performance for novel scenes by about 48 percent. The theory on slow-wave oscillations relating to memory retention is that new sensory information is initially encoded in the hippocampus of the brain for short-term storage. Then, because they can be quickly forgotten, the memories are transferred during sleep from the hippocampus to the cerebral cortex where they are integrated and consolidated with previous knowledge. This enables the new knowledge to be remembered and generalized better, increasing retention of new skills for longer periods. "The processes we affected with noninvasive electrical stimulation are slow-wave oscillations of the brain's electrical field that occur during non-REM sleep stages II and III. We tracked ongoing oscillations and applied tACS that matched their frequency and phase in the slow-wave oscillation band. This matching is what we mean by a closed-loop system. The technique is unique to Hrl," said Praveen Pilly, Hrl's principal investigator. In the experiment, subjects had tACS applied or not applied (sham group) during sleep overnight. Their performance on the task was then measured over time to detect persistence of enhanced learning. Titled "Closed-loop slow-wave tACS improves sleep dependent long-term memory generalization by modulating endogenous oscillations," the paper was published in the July issue of *Journal of Neuroscience*.

AI could predict medication response in patients with complex mood disorders

Mood disorders like major depressive disorder (MDD) and bipolar disorder are often complex and hard to diagnose, especially in youth when the illness is just evolving. This can make decisions about medication difficult. In a collaborative study by Lawson Health Research Institute, The Mind Research Network and Brainnetome Center, researchers have developed an artificial intelligence (AI) algorithm that analyzes brain scans to better classify illness in patients with a complex mood disorder and help predict their response to medication. The full study included 78 emerging adult patients from mental health programs at London Health Sciences Centre. The first part of the study involved 66 patients who had already completed treatment for a clear diagnosis of either MDD or bipolar type I (bipolar I), as well as an additional 33 research participants with no history of mental illness. Each individual participated in scanning to examine different brain networks using functional magnetic resonance imaging (fMRI). The research team analyzed and compared the scans of participants and found the three groups differed in particular brain networks. These included regions in the default mode network, a set of regions thought to be important for self-reflection, as well as in the thalamus, a 'gateway' that connects multiple cortical regions and helps control arousal and alertness. The data was used by researchers at The Mind Research Network to develop an AI algorithm that uses machine learning to examine fMRI scans to classify whether a patient has MDD or bipolar I. When tested against the research participants with a known diagnosis, the algorithm correctly classified their illness with 92.4 percent accuracy. The research team then performed imaging with 12 additional participants with complex mood disorders for whom a diagnosis was not clear. The research team hypothesized that participants classified by the algorithm as having MDD would respond to antidepressants while those classified as having bipolar I would respond to mood stabilizers. When tested with the complex patients, 11 out of 12 responded to the medication predicted by the algorithm. The study, "Complexity in mood disorder diagnosis: fMRI connectivity networks predicted medication-class of response in complex patients," was published online Aug. 6, 2018, in *Acta Psychiatrica Scandinavica*.

Brain proteins, patterns reveal clues to understanding epilepsy

New therapies could be on the horizon for people living with epilepsy or anxiety, thanks to a breakthrough discovery by University of Nevada-Las Vegas, Tufts University School of Medicine, and an international team of researchers studying how proteins interact to control the firing of brain cells. The study, published Aug. 7, 2018, in *Nature Communications* under the title "Developmental seizures and mortality result from reducing GABAA receptor α2-subunit interaction with collybistin," provides new insight into ways to regulate a specialized "compartment" of cells in the brain that controls their signaling. If scientists and doctors can influence that compartment, they can control the firing of brain cells, which may in turn stop or prevent seizures, among other things. The six-year project moved one step closer to answering decades-old questions about brain wave control, by quantitatively defining how two key proteins – the GABAA receptor α2 subunit and collybistin – interact. When the interaction was disrupted in rodent models, EEG tests showed brain waves moving out of control, mimicking patterns seen in humans with epilepsy and anxiety. Coordinating the research effort was Stephen Moss, professor of neuroscience at Tufts and director of the Astrazeneca Laboratory for Basic and Translational Neuroscience in Boston. Moss said that the study results should stimulate the development of drugs that target the GABAA receptor α2 subunit as new, more effective treatments for epilepsy.