

December 2020 Issue 14

Highlights

- Physica Medica Focus Issue published
- New paper on pioneering new cancer radiotherapy
- Cosylab to provide the control software of Australia's first proton therapy unit
- Partner News

Onwards and upwards to a brighter 2021!

2020 has been an eventful and no doubt very challenging year for all of us and I am sure that you will all be looking forward to the upcoming break. It is hard to believe that it has been almost one year that our OMA project has come to an end, in particular as there are still so many visible results from the network: Fellows completing their PhDs, papers on their OMA projects being published, as well as whole collections of papers, for example in the European Journal of Medical Physics, Physica Medica. I already announced a special issue on the basis of our OMA Conference on Medical Accelerators and Particle Therapy in our last OMA Express, but wanted to point out that a number of additional papers have now been published. A paper on FLASH proton therapy is even amongst the most downloaded

papers in this journal – so please make sure you have a look!

With the approval of the COVID vaccine, there is now a glimmer of hope that 2021 can see us return to a more normal life. Whilst there are no doubt benefits in working from home and cutting down on travel through online meetings, it is also clear that technology cannot fully reproduce the benefits from face-to-face contact and detailed in-person discussions. Through our OMA events over the years, networking has been a central element of our successes and we are keen to organize in-person workshops for our community as soon as we can safely do so.

I wish you and your families a safe end to this challenging year, a wonderful Christmas time and good start into a hopefully much better 2021!

Prof. Carsten P. Welsch Coordinator

Research News

New paper published that provides basis for in-vivo range verification

EPJ Web of Conferences

carbon Protons and ions have been extensively used for radiotherapy treatments, and in comparison to conventional radiotherapy, they allow a more conformal dose to the target tumour, especially in case of deep-seated tumours.

However, the accuracy of hadron therapy treatments is affected by uncertainties in the particle range calculations. Several techniques are under development for in-vivo range verification, one of which consists on measuring the activity distributions of positron emitters, such as 10C, 11C and 15O, which are produced in the patient body during proton and carbon ion treatments.

In a paper that has just been published in EPJ Web Conf 239, OMA Fellow Giulia Aricò and co-workers present a comparison between measured and expected positron emitter activity distributions. They show how this can provide information on the quality of the delivered treatment and accuracy of the particle range calculations.

In their work the FLUKA production cross sections for 10C, 11C and 15O originated from proton and carbon ion beams in carbon and oxygen targets were compared with experimental data, at low and therapeutic energies.

Their study highlights that some improvements in the FLUKA physics models can be performed in order to achieve an even

better agreement with the experimental production cross sections. The effects of such improvements on the activation yields and profile distributions will finally have to be assessed in clinical scenarios. This research is then expected to contribute to a further improvement of radiotherapy treatment at CNAO, where FLUKA is used as reference for PET measurements.



Production cross sections for 10C originated from proton beams in carbon and oxygen targets as a function of energy. The black filled dots are FLUKA simulations, the green empty symbols are data from the Experimental Nuclear Reaction Data (EXFOR) library, and the blue empty circles are data from Phys. Med. Biol. 64 205012 (2019). Image taken from referenced paper.

G. Arico, et al., "Benchmarking of FLUKA production cross sections of positron emission tomography isotopes for in-vivo range verification in hadron therapy", EPJ Web Conf 239 (2020) https://doi.org/10.1051/epjconf/202023924001







Physica Medica Focus Issue published

Physica Medica, European Journal of Medical Physics, provides an international forum for research and reviews in areas such as medical imaging, radiation therapy, as well as education and training in medical physics. The journal has just published a Focus Issue on the Optimization of Medical Accelerators. The Focus Issue presents research highlights from the International Conference on Medical Accelerators and Particle Therapy that was organized in Seville, Spain by the Optimization of Medical Accelerators (OMA) network.

The OMA project has joined universities, research centres and ion-beam treatment facilities together with leading industry partners, to address the challenges in cancer treatment facility design and optimization, numerical simulations for the development of advanced treatment schemes, beam imaging and treatment monitoring.

The network has been built around 15 early stage researchers (ESRs) working on dedicated projects to maximize the benefits of the use of particle beams for cancer treatment. The network consists of an international consortium of 38 partner organizations working in this field. It has provided a cross-sector interdisciplinary environment for beyond state-of-the-art research, researcher training, and new collaborations.

The conference provided an opportunity for all the Fellows to present their research outcomes to the medical accelerator community. It featured invited talks from research leaders, contributed talks and poster contributions, attracting more than 70 delegates from all around the world. The Focus issue presents key findings in areas such as range determination, novel diagnostics including cavity resonators, dose delivery systems for treating moving targets, and FLASH proton therapy.

All articles can be accessed via this website: https://www.sciencedirect.com/journal/physi ca-medica/special-issue/10T41HWXWLV

Enhancing cancer treatment through beam transport optimization

A paper presenting a comprehensive study of the <u>Clatterbridge Cancer Centre(CCC)</u> proton beam therapy facility has been published in the European Journal of Medical Physics (Physica Medica) by OMA Fellow Jacinta Yapand colleagues from CCC, UCL and John Adams Institute/RHUL. CCC is the world's first hospital based proton beam therapy facility and has been treating ocular cancers since 1989. Over the past years, the facility has supported a strong research programme covering several challenges within particle therapy, including detector development and radiobiological studies. Proton therapy is an advanced modality of radiation therapy which utilises a beam of protons to safely and precisely deliver radiation to tumour volumes. The physical characteristics of protons and the combination of technologies which deliver and shape the beam, allow the dose to be concentrated at the specific site of the tumour whilst minimising radiation to surrounding healthy tissue. In recent years there has been a rapid growth in the number of clinics being built around the world, particularly centres which treat at higher energies (> i.e. 160 MeV). This allows the





beam to penetrate further into the body and deliver radiation to deeper seated tumours. However, earlier built facilities continue to treat for certain candidates, including uveal melanomas which have the highest incidence rate for adult eye cancers. Proton therapy is the gold standard treatment for eye tumours: CCC is a pioneering facility and one of a few dedicated ocular clinics in the world.

As such, different facilities have varying treatment requirements depending on a multitude of factors. Ultimately, the beam is generated and delivered as a result of several considerations including, the facility design, accelerator, beam transport, beam diagnostics and delivery technique. These aspects are often well known at modern facilities however may be limited for those built earlier, including CCC which is a unique facility. Therefore, a complete investigation was performed to characterise the facility in order to better utilise the capabilities of the beamline for research and experimental work.



OMA Fellows Jacinta Yap and Navrit Bal during a visit to CCC in 2019.

Jacinta said: "This paper overviews the beam dynamics studies of the Clatterbridge proton therapy ocular facility, for accurate simulations and end-to-end characterisation of the beamline. As several particle therapy related experiments and studies are performed at Clatterbridge, this work aims to provide a better understanding of the accelerator, transport and delivery of the beam as well as additional tools for improved modelling capabilities."

An extensive review was carried out to retrieve beamline information restricted by facility related uncertainties and to accurately define the magnetic elements. These transport the beam from the cyclotron (source) to the treatment room and must be accurately defined. To account for various limitations, the magnetic parameters were optimised and a nominal case was implemented which would best represent the present day conditions of the facility. This information is defined in an optical lattice which was modelled in two codes (MAD-X) and (BDSIM) to simulate the behaviour, transport and distribution of the beam.

Therefore, the Twiss parameters, transmission, phase space and size of the beam could be known anywhere along the beamline, enabling end-to-end characterisation. These provided the definition of the beam at the start of the treatment room and were used in a simulation model of the delivery system built in another code (TOPAS). The transverse beam profiles were simulated and compared to measurements with EBT3 Gafchromic film. Similarities between the two distributions demonstrate the applicability of the input beam parameters derived from the developed optical lattice.

The paper presents an approach to retrospectively characterise a proton therapy facility and develop computational models for accurate simulations. This work provides an overview of the beam dynamics of the CCC beamline as useful for upgrades, integration of diagnostics, research work and may also be similarly applied at other facilities.

Jacinta Yap, et al., "Beam characterisation studies of the 62 MeV proton therapy beamline at the Clatterbridge Cancer Centre", Physica Medica, Volume 77, September 2020, 108-120 https://doi.org/10.1016/j.ejmp.2020.08.002





Geometry of an energy degrader in a cyclotron-based proton therapy facility

In a cyclotron-based proton therapy facility, the fixed extraction energy of protons is reduced downstream of the accelerator source to the energy range required by the treatment plan. Most typically, an energy degrader made of a robust material, i.e., graphite, of variable thickness is inserted into the beamline. The beam passing through the absorber material undergoes the ionisation slowing, but also acquires a larger emittance due to the multiple Coulomb scattering. The degrader is hence followed by a set of collimators to select an appropriately small portion of the beam to be transported to the patient. Such a system introduces beam losses that significantly vary depending on the exit energy; at 70 MeV the transmission from the cyclotron to the isocentre can be as low as 0.1%.

including OMA Fellow А team Ewa **Oponowicz** examined three different geometries of a graphite degrader: multiple wedges, multiple slabs and a single block, of equivalent total thickness, to determine which arrangement minimises the beam losses. Measurements of the PROSCAN beamline with the conventional multi-wedge degrader at the Proton Therapy Centre at Paul Scherrer Institute (Switzerland) were used to validate the Monte Carlo simulations. Careful calculations of the emittance at the degrader exit were necessary to reliably compare the three cases.



Ewa Oponowicz at PSI.

Ewa said: "These were very fruitful studies; they mainly focused on various geometries of the energy degrader, but also prompted considerations on careful emittance calculations and motivated a new experimental method to determine the material ionisation potential."

The researchers determined that a solid block case delivers significantly larger particle transmission for the entire range of treatment energies, and up to 17% larger at 150 MeV. They therefore concluded that a single block degrader is the geometry that should be considered in cyclotron-based proton therapy systems to improve the overall beam transmission. Further studies into optimisation of the degrader performance are ongoing and focus on novel materials, such as boron carbide B4C.

Oponowicz, E., H. L. Owen, S. Psoroulas, and D. Meer. "Geometry optimisation of graphite energy degrader for proton therapy.", Physica Medica 76 (2020): 227-235. DOI: 10.1016/j.ejmp.2020.06.023





First non-interceptive beam current measurement at the proton therapy facility PROSCAN

At PSI's proton therapy facility PROSCAN, researchers including OMA Fellow <u>Sudharsan</u> <u>Srinivasan</u> have successfully demonstrated for the first time non-interceptive beam current measurement in the range 0.1-10 nA over the energy range 238-70 MeV, using a dielectric-filled reentrant cavity resonator. This newly developed cavity operates with a so-called TM_{010} mode, also referred to as monopole mode, and is a realization from the lumped element model shown below. Beamline measurements were performed and compared to a reference ionization chamber.

B4C.



Dielectric-filled reentrant cavity resonator with induced E and B fields in the separate capacitive and inductive zones

A good agreement between the measured resonator sensitivity with the expected trend

of sensitivity as a function of energy was found as indicated in the plot below.



Dielectric-filled reentrant cavity resonator with induced E and B fields in the separate capacitive and inductive zones

Sudharsan commented: "Our measurements have underlined the excellent potential of this cavity resonator to replace ionization chambers for beam current measurements at proton therapy facilities. "

The PSI cavity resonator will now be tested as a tool for beam control optimization; it's comparably long signal integration time make it a promising complementary measurements that provides deeper insight into the characteristics of the beam.

S Srinivasan, P-A Duperrex, J M Schippers, "Beamline characterization of a dielectric-filled reentrant cavity resonator as beam current monitor for a medical cyclotron facility", European Journal for Medical Physics (2020) https://doi.org/10.1016/j.ejmp.2020.09.006





Modular, motion-synchronized delivery of conformal treatment plans

The motion team within the Biophysics department at GSI joined forces with CNAO, in Pavia Italy, to implement a sophisticated strategy for delivering conformal radiation volumes to moving tumors.

Most recently, Michelle Lis, an early stage researcher at GSI within the OMA project, has developed the first version of a modular dose-delivery system (DDS) for scanned-ion radiotherapy that mitigates against organ motion artifacts by synchronizing the motion of the ion beam with that of the moving anatomy. This unique approach is a step away from conventional methods, which seek to suppress tumor motion, or that attempt to [continuously track and guide the beam movement]. "We found that conventional approaches, like the tracking method, introduce other problems and can't really account for all the complexities of respiration, but I think that the motion-synchronized dose delivery strategy that we developed is one that is so versatile and expandable that it can do it."



Illustration of treatment process, courtesy GSI.

Michelle integrated a new motion synchronization system into the DDS existing at CNAO and a copy found at GSI. The DDS is a modular devise, so integration into the GSI environment was possible with just an adaptive layer of software and hardware interfaces.

The method of synchronization comprised three major tasks.

1. The creation of a set of 3D treatment plans, where each corresponds to one phase of respiratory motion and together comprises a 4D plan library.

2. Monitoring anatomic motion during treatment.

3. Synchronizing the ion beam scanning to the detected anatomic motion.

The synchronization was accomplished in real time by repeatedly selecting and delivering an ion beam spot within a 3D plan (the one that most closely corresponded to the current anatomic state) until all plans were delivered. The performance characteristics of the motion synchronization system were tested at both GSI and at CNAO by delivering 4D treatment plans to a moving phantom. Recently, Michelle and her group have published a manuscript describing the results of their initial performance tests. This manuscript, entitled "A modular dose delivery system for treating moving targets with scanned ion beams: performance and safety, characteristics and preliminary tests" has been published in the Physica Medica Journal. With this work, she has demonstrated, for the first time, that a modular prototype system, can synchronize scanned ion beams with moving targets to deliver conformal, motion-





compensated dose distributions. The M-DDS will be further enhanced to treat irregular motion patterns. The system will then undergo extensive safety testing before translating to the clinic.

"Developing a novel method for treating moving tumors has been a wonderful experience. I am proud to contribute to the development of better cancer treatment methods." After the conclusion of her PhD, Michelle will continue to work in Radiation Oncology, and plans to pursue a career in industry.

M. Lis, et al., "A modular dose delivery system for treating moving targets with scanned ion beams: Performance and safety characteristics, and preliminary tests", EJMP Physica Medica 76, pp 307-316 (2020). https://doi.org/10.1016/j.ejmp.2020.07.029

New paper on pioneering new cancer radiotherapy

FLASH radiotherapy is a promising new technique that uses high-energy particles to treat tumors; a high dose of radiation is administered almost instantaneously – in milliseconds rather than around a minute. Here, the tumor tissue is damaged in the same manner as with conventional radiotherapy. However, it is believed that healthy tissue is less affected, meaning that less side effects are expected.

The aim is a step change in cancer treatment, and there is a growing interest in the proton therapy community, with early tests indicating that the FLASH effect is present with high dose rate proton irradiation as has been observed with conventional X-ray treatments.

A paper by S Jolly from UCL and co-workers from several other OMA partner institutions has just been published in Physica Medica (European Journal of Medical Physic) and is already one of the most downloaded papers from EJMP. It focuses specifically on the technological challenges of FLASH proton therapy. In fact, the delivery of FLASH proton therapy requires significant advances in accelerator, magnet, beam diagnostics and dosimetry technology.

Researchers across OMA institutions are working on these. Different accelerator types are being considered for the delivery of the proton beam and each one has its own challenges in order to meet this goal.

The authors show that the most direct route to a clinical FLASH proton system appears to be with an isochronous cyclotron utilizing a hybrid spot-scanned approach. However, significant changes in the mode of operation or treatment using either this accelerator type, or instead using synchrotrons or linear accelerators, will be needed in order to enable a fully-fledged FLASH system. To design optimal technology for such a system, further studies are also required on the biological and clinical issues; the CI is engaged in several international collaborations with industrial partners to realize this goal.

S. Jolly et al., "Technical challenges for FLASH proton therapy", Physica Medica – EJMP 78, p71-82 (2020) https://doi.org/10.1016/j.ejmp.2020.08.005





Fellows Activity

PhD completed – Anna Vnuchenko



On 19 June 2020, OMA Fellow Anna <u>Vnuchenko</u> successfully defended her PhD thesis. Her doctoral thesis was evaluated during the act of defence which took place in a public session online due to the COVID pandemic. Despite these obstacles, the defense was successful and the thesis received a special mark of honour: "Cum laude".

The title of Anna's work is "High-gradient issues in S-band rf accelerating structure for hadron therapy accelerators and radio frequency quadrupoles". This OMA project was hosted by CSIC/IFIC – Instituto de Fisica Corpuscular in Spain. Anna has been a student in the Faculty of Physics - Department of Applied Physics and Electromagnetism at University of Valencia.

Anna's thesis focused on the study of highgradient limitations in normal conducting radio-frequency (rf) accelerating structures. It has a focus on rf vacuum breakdowns that occurs due to the high electromagnetic fields found in such structures. Her thesis describes in detail the achieved performance and longterm behaviour of different types of accelerating structures, including RFQs that can be used for medical accelerators. Her work has demonstrated that an all-linac facility for hadron therapy based on highgradient technology is now a perfectly feasible approach.

Her work also gave important indications about the main characteristics required by state-of-the-art test benches. Her R&D will no doubt be very useful for future studies into breakdown behaviour of various accelerating structures.



Research in this area continues after the end of her OMA project in collaboration between IFIC-CSIC, the CERN RF CLIC group and CERN's knowledge transfer group. Her experimental work related directly to high-gradient testing of a medical linac structure designed for proton therapy and results have recently been published in the journal Physical Review Accelerators and Beams.

Following onto her OMA Fellowship, Anna now continues her scientific career as a Fellow at CERN where she is working on the optimization of the negative ion source for CERN's LINAC4.

Congratulations!

A. Vnuchenko, et al., "High-gradient testing of an S-band, normal-conducting low phase velocity accelerating structure", Phys Rev AB 23, 084801. https://doi.org/10.1103/PhysRevAccelBeams.23.084801





Partner News

Cosylab to provide the control software of Australia's first proton therapy unit



Radiance 330 treatment room. (Image courtesy of Cosylab)

OMA partner <u>Cosylab</u> has spent the last four years actively developing, fine-tuning and integrating the Treatment Delivery Control System and the Motion Control System for the Radiance 330 Proton Therapy System in close collaboration with <u>ProTom</u> International.

The new Australian Bragg Centre in Adelaide, which is the first proton therapy unit in Australia, has now chosen ProTom's Radiance 330 device as its functional core and, with it, Cosylab's embedded systems-software.

The Australian Bragg Centre will treat an estimated 600 to 700 patients each year when it becomes fully operational at the end of 2024.

The Radiance 330 PT system utilizes an integrated imaging and control system, and advanced pencil-beam scanning technology. The latter is one of the most advanced forms of proton therapy treatment, as it enables the system to apply superior dose sculpting and higher beam efficiencies than other methods of proton therapy. Pencil-beam scanning technology also reduces the adverse side-effects to patients and improves their long-term outcome and quality of life.

Thus Cosylab has participated in the successful development of one of the smallest and lightest proton therapy systems on the market which is based on a very compact synchrotron particle accelerator.

OMA Coordinator continues to lead Liverpool physics

OMA Coordinator Professor Carsten P Welsch has just been confirmed for a second 5-year term as Head of the Physics Department at the University of Liverpool. During his first term, his Department saw a number of improvements, including a major refurbishment of its Oliver Lodge building, a steady increase in its undergraduate and postgraduate student numbers, new academic appointments, industrv and research centre partnerships, as well as major international events that were hosted in Liverpool. Congrats!





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Future Circular Collider film wins Silver in W3 Awards



On 6th October 2020 the Winners of the 15th annual w3 Awards have been announced by the Academy of Interactive and Visual Arts. Receiving over 3,000 entries from across the globe, the w3 Awards honour outstanding Websites, Marketing, Video, Mobile, Social, and Podcasts created by some of the best digital content creators across the industry.

The film "Future Circular Collider" which the University of Liverpool has produced with CERN and Polar Media has been named a Silver Winner in the category Branded Entertainment - Science & Technology. The film was co-created by OMA Coordinator Professor Carsten P Welsch who said: "It was an exciting experience to produce this film with our fantastic partners at CERN and Polar Media. It carries an important message about the future of discovery science, the need for technological innovation and the importance of international collaboration. Personally, I particularly enjoyed the filming with Nobel Laureate Peter Higgs at the Royal Society of Edinburgh."

The video explains how a Future Circular Collider (FCC) could open a window for exploring the unknown 95% of the universe and help answer many fundamental questions: What is dark matter? Are there supersymmetric particles? Are there other fundamental interactions? It also describes the numerous challenges that are being tackled by the FCC collaboration.

Please follow the link to watch the awardwinning film.

https://youtu.be/Uvq8vF5LKzM







The Economics of Big Science

Investment in science – whether in education and training or through public funding for developing new research tools and technologies – is crucial for progress. In a book that was just published as part of Springer's Science Policy Reports, authors from big research laboratories and organizations, funding agencies and academia discuss how investing in science can produce societal benefits, as well as identifying future challenges for scientists and policy makers.

The volume cites different ways to assess the socio-economic impact of Research Infrastructures and their role as hubs of global collaboration, creativity and innovation. It highlights the different benefits stemming from fundamental research at the local, national and global level, while also inviting us to rethink the notion of "benefit" in the 21st century.

Public investment is required to maintain the pace of technological and scientific advancements over the next decades. The authors discuss ways for maintaining a strong foundation of science and research to ensure that we continue to benefit from the outputs. The volume draws inspiration from the first "Economics of Big Science" workshop which was held in Brussels in June 2019 with the aim of creating a new space for dialogue and interaction between representatives of Big Science organizations, policy makers and academia.

OMA Coordinator and Liverpool's Head of Department Prof Dr Carsten P Welsch contributed to the book and his chapter highlights how fundamental science has driven revolutionary transformations of technology and society. He also describes how 'training the next generation' is a very important drivers of science and economic progress. He said: "Public investment in curiosity-driven research (...) provides an important stimulus for innovation as R&D companies tend to concentrate around vibrant scientific communities that provide much-needed talent. By renewing and strengthening investment in basic science, the way to an even brighter future can be paved." You can access the full book in Open Access format here:

https://link.springer.com/book/10.1007/978-3-030-52391-6



The Economics of Big Science Essays by Leading Scientists and Policymakers Foreword by Rolf-Dieter Heuer

🙆 Spi

OMA consortium announces accession of new partner

The OMA consortium would like to welcome the <u>University of Melbourne</u> as newest partner. Australia's leading university can look back at a rich and fascinating past spanning 160 years. Today over 8,000 academic and professional staff support a vibrant student body of more than 48,000, including more than 13,000 international students from over 130 countries around the world.

The Medical Accelerator Physics group at the University of Melbourne was created in 2019 as the first academic accelerator physics group in Australia. The group vision is to bring positive benefits to society through the development of particle accelerators and their applications, particularly in the medical domain.

Current projects at Melbourne University span from next-generation hadron therapy accelerator and gantry designs using both synchrotron and fixed-field alternating gradient accelerator technology to the development of robust linear accelerators for radiotherapy in Low and Middle-Income countries.

Welcome!







Selected Publications

Benchmarking of FLUKA production cross sections of positron emission tomography isotopes for invivo range verification in hadron therapy

Giulia Aricò, Giuseppe Battistoni, Francesco Cerutti, Felix Horst, Andrea Mairani, Christoph Schuy, Uli Weber and Alfredo Ferrari, EPJ Web Conf 239 (2020)

<u>Beamline characterization of a dielectric-filled reentrant cavity resonator as beam current monitor</u> <u>for a medical cyclotron facility</u>

Sudharsan Srinivasan, Pierre-André Duperrex, Jacobus Maarten Schippers, Physica Medica 78 (2020): 101-108.

<u>Technical challenges for FLASH proton therapy</u> Simon Jolly, Hywel Owen, Marco Schipper, Carsten Welsch, Physica Medica 78 (2020): 71-82.

Beam characterisation studies of the 62 MeV proton therapy beamline at the Clatterbridge Cancer Centre

Jacinta Yap, Javier Resta-López, Andrzej Kacperek, Roland Schnuerer, Simon Jolly, Stewart Boogert, Carsten Welsch, Physica Medica 77 (2020): 108-120.

A modular dose delivery system for treating moving targets with scanned ion beams: Performance and safety characteristics, and preliminary tests'

Michelle Lis, Marco Donetti, Wayne Newhauser, Marco Durante, Joyoni Dey, Ulrich Weber, Moritz Wolf, Timo Steinsberger, Christian Graeff, Physica Medica 76 (2020):307-316.

Geometry optimisation of graphite energy degrader for proton therapy

E. Oponowicz, H. L. Owen, S. Psoroulas, and D. Meer. " Physica Medica 76 (2020): 227-235.









NOTICE BOARD

DEADLINE FOR THE NEXT NEWSLETTER 15th March 2020

The newsletter is published on a quarterly basis. Help us keep it interesting by providing your news and updates.



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