

OUTLOOK

Visions and research directions for the Wireless World

A New Generation of e-Health Systems Powered by 5G



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WWRF WG e/m-Health and Wearables Vertical Industries Platform (VIP)

White Paper

“A New Generation of e-Health Systems Powered by 5G”

Chief Editor:

Christos Politis

Contributing Editors:

Christoph Thuemmler, Nikolaos Grigoriadis, Pantelis Angelidis, Nigel Jefferies, Bin Zhen, Guixia Kang, Cindy Fedell, Clara Li, Chunxue Bai, Kostas Danas, Katarzyna Wac, Panayiotis Ketikidis

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Project website address: www.wwrf.ch

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Executive Summary

Standardized 5G systems will be market ready around 2020. What is clear is that 5G will be more than a simple evolution of the current network. Indeed, it will be a catalyst for new products and services by integrating networking, computing and storage resources into a unified infrastructure, becoming the nervous system of cognitive objects and cyber-physical systems.

WWRF has devised a series of vertical industry platform (VIPs) for 5G, where important standardization topics can be seeded and cultivated. This white paper has as its scope the requirements of providing effective healthcare using 5G technology. This will be a springboard for further work, including recruitment and use of a panel of experts to take part in a Delphi study to refine these conclusions, becoming a living document.

A word-cloud analysis showed that phrases such as IoT, spectrum and infrastructure predominate in industry white papers. Phrases such as QoS or QoE are mentioned infrequently, but 'low latency' and reliability seem more important. Few real end-users of e-Health and medical applications were consulted in other studies. The small form factor of many medical devices is a significant challenge, particularly for wireless design. Overall 5G requirements are still evolving, as vertical industries become increasingly engaged in the process. Though, one requirement that has not been fully developed is time synchronization.

Health 4.0 is a vision of care delivery that is distributed and patient-centered, and there is already evidence of a shift towards virtualization and individualization of care. With 5G as its foundation, the transition to person-led care can be completed. Healthcare models are rapidly changing due to demographic and socio-economic changes from a hospital based, specialist focused approach to a distributed patient centric care model. The point of care is shifting from hospitals towards GP surgeries, day-clinics, care homes, patient homes and the Internet.

The empowerment of patients and their formal and informal carers has become a prime target of healthcare strategy development in Europe and elsewhere. Emerging new network technologies (LTE, 5G) allowing for SDN and NFV will form the backbone of future healthcare, enabling the Internet of Things, Smart Pharmaceuticals and Individualized Medicine. Cloud computing, Big Data and enhanced security will enable virtualization and individualization of care and allow the application of Industry 4.0 design principles in health care (Health 4.0).

1. Introduction

Previous generations of mobile communication systems have evolved, from analogue speech-based systems to the high-speed data-orientated networks being rolled out under the '4G' banner. In June 2015, ITU-R officially released the naming, usage scenarios and requirements of 5G (IMT-2020). Among the three usage scenarios (enhanced mobile broadband, massive machine-type communications and ultra-reliable & low-latency communications) defined by ITU-R, the latter two are particularly suited to support vertical industry applications.

However, the introduction of vertical industries into the telecom network will not be straightforward, as industry sectors have different knowledge sets and speak in different technical languages. These gaps between the telecom and vertical industries have become a stumbling block on the road towards 5G. To address this challenge, WWRF has devised a platform called the vertical industry platform (VIP) for 5G. WWRF is the unique global forum that brings together industry and academia to address research and other challenges to developing a really wireless world. The Forum is planning on creating more VIP working groups to address the different vertical industry applications including connected vehicles, smart metering, home automation and so on.

The VIP is a pre-standards platform where important standardization topics related to vertical industries will be seeded and cultivated. The scope of this paper is the requirements of providing effective healthcare on 5G technology, and the identification of use cases for 5G in the healthcare system.

The specific objectives of this paper are to develop WWRF as a bridge between the people, organizations and industries involved in healthcare and the 5G standards organizations (such as 3GPP) to gather their requirements and prepare for standardization, to create better understanding of the potential and capabilities of 5G and enable those involved to jointly discuss the vision, usage scenarios, requirements and enabling technologies to achieve the targets of future vertical industry communications in 5G.

Although working alongside the 5GPPP research programme in Europe, and the ongoing standardization activity in 3GPP SA1, the scope of WWRF's work includes looking beyond current activities to help set a technology roadmap for the future. To this end, the initial release of this WWRF Outlook will be the springboard for further work, including the recruitment and use of a panel of experts to take part in a Delphi Study to refine the conclusions of this release. So the Outlook will be come a living document, with version 2.0 to be released in early-2017 containing the results of the Delphi Study, and Version 3.0 at the end of the year reporting on the first implementation scenarios and results of selected projects.

2. Meta-analysis of existing white papers

With the past four generations of mobile technology, each generation has extended the network capabilities and enhanced the user experience compared to its predecessors. Historically, from the first to the 4th generation, the vision and development of mobile communication has been centred in North America, Europe and Asia. Following this, the global wireless community has clustered at 3GPP and ITU to develop the standards. It is generally assumed that commercial standardized 5G mobile communication systems will emerge around 2020.

However, in the second half of 2016, there is still no clear definition of, or detailed requirements for, 5G systems. Identifying those expectations and mapping them to the corresponding technology components is a key activity for the 5G initiatives. Across the world, it is generally agreed that 5G will be more than an evolution of the current network to connect humans, where the network is a mere pipe of bits.

More significantly, 5G will provide an infrastructure for society to face the challenges of economic and society transformation, which have never been experienced before. In the EU and Asia, an aging population will mean higher healthcare costs, given the current hospital- and doctor-centric medical system. With the new types of terminal devices, such as wearables, smart watches, augmented and virtual reality devices, smart phones and tablets, user habits and expectations of media consumption are likely to be more interactive. Manufacturing procedures will be integrated into the whole logistic and production value chain. Autonomous and cooperative vehicles are bringing new levels of road safety and traffic efficiency, digital transport and logistics, as well as a broad range of new business opportunities.

The 5G will be a catalyst to trigger innovation of new products and services for all these new vertical industries by integrating networking, computing and storage resources into one programmable and unified infrastructure. Table I lists the landscape of global 5G vertical usage cases and requirements definitions. All researches clearly show that 5G network will become the nervous system of cognitive objects and cyber-physical systems, which enable services to everyone and everything.

Organizati on/project	Publication times	Members	Region	Major vision of vertical applications
METIS	I (Apr./2013)	Telecomm- operators, vendors, academic researchers	EU	Ubiquitous things communications, super- real time and reliable communications
	II (Jan./2016)			Massive MTC (sensors and actuators), ultra- reliable MTC (Connected cars)
IMT-2020	May/2014	Government, telecomm- operators, vendors, academic researchers	China	low-power massive connections, low-latency high-reliability connections (Internet of Vehicles and industrial control)
4G Americas	Oct./2014	Telecomm- operators, vendors,	US	Smart grid and critical infrastructure monitor, smart cities, m-Health and telemedicine, automotive, sports and fitness
NGMN	Dec./2014	Telecomm- operators	Global	Massive IoT, broadcast- like service, ultra-reliable communication, extreme real-time communications
Future Forum	Jan./2015	Telecomm- operators, vendors, academic researchers	China	Wearable devices, smart machines (drone, robots, cars), wireless sensors
5GPPP	May - Oct./2015	Telecomm- operators, vendors, academic researchers, verticals (car, manufacturers)	EU	e-Health, Smart grid and energy, Automotive, factory of future, media and entertainment
ITU-T	Sep./2015	Government, telecomm- operators, vendors	Global	Massive connection (smart city), ultra-reliable and low latency connection (industry automation, self- driving car)
3GPP SA1 SMARTER	Nov./2015	Telecomm- operators, vendors	Global	Massive MTC, critical communication, enhanced V2X,
5G Forum	Mar./2016	Telecomm- operators, vendors	Korean	Massive connectivity, V2X communication

EU-China joint white paper on the Internet of Things	Jul./2016	Government, academic, researchers	EU, China	Industrial manufacturing, agriculture, energy and environmental, smart city, health care, pipe network monitoring, intelligent transportation,
5GMF	Jul./2016	Government, telecomm-operators, vendors academic researchers, verticals (broadcast, transportation)	Japan	Self-driving vehicle, IoT (industrial, wearable, agriculture), Artificial Intelligence and robots

Table 1¹: Global activities of 5G vertical usage cases and requirements definition

With the past four generations of mobile technology, each generation has extended the network capabilities and enhanced the user experience compared to its predecessors. Historically, from the first to the 4th generation, the vision and development of mobile communication has been centred in North America, Europe and Asia. Following this, the global wireless community has clustered at 3GPP and

¹ The following references were used to built this table:

- Future Forum, "5G White Paper V2.0: rethink mobile communications for 2020+", (<http://euchina-ict.eu/wp-content/uploads/2015/01/5G-SIG-white-paper-first-version.pdf>)
- 4G America, "4G America's recommendations on 5G requirements and solutions," (http://www.4gamericas.org/files/2714/1471/2645/4G_Americas_Recommendations_on_5G_Requirements_and_Solutions_10_14_2014-FINALx.pdf)
- 5G forum, "5G Vision, Requirements, and Enabling Technologies," (<http://kani.or.kr/5g/whitepaper/5G%20Vision,%20Requirements,%20and%20Enabling%20Technologies.pdf>)
- IMT-2020, "5G Vision and Requirements"
- 5GMF "5G Mobile Communications Systems for 2020 and beyond,"
- 5G-PPP "5G and eHealth" (<https://5g-ppp.eu/white-papers/>)
- METIS I, "Deliverable D1.1 Scenarios, requirements and KPIs for 5G mobile and wireless system," (https://www.metis2020.com/wp-content/uploads/deliverables/METIS_D1.1_v1.pdf)
- METIS II, "Deliverable D1.1 Refined scenarios and requirements, consolidated use cases, and qualitative techno-economic feasibility assessment," (https://metis-ii.5g-ppp.eu/wp-content/uploads/METIS-II_D1.1_v1.0.pdf)
- NGMN, "NGMN 5G white paper," (https://www.ngmn.org/uploads/media/NGMN_5G_White_Paper_V1_0.pdf)
- 3GPP, "3GPP Technical Specification Group Services and System Aspect: Feasibility Study on New Services and system, Stage 1" (<http://www.3gpp.org/DynaReport/22891.htm>)
- ITU-R M.2083-0, "IMT Vision – Framework and overall objectives of the future development of IMT for 2020 and beyond," (https://www.itu.int/dms_pubrec/itu-r/rec/m/R-REC-M.2083-0-201509-!!!PDF-E.pdf)
- EU-CN Internet of Things White Paper, (<https://ec.europa.eu/digital-single-market/en/news/eu-china-joint-white-paper-internet-things>)

ITU to develop the standards. It is generally assumed that commercial standardized 5G mobile communication systems will emerge around 2020.

Figure 1 shows a word-cloud analysis of the 5G vertical usage cases and requirements. The highly ranked *IoT*, which appears even more frequently than key word *video*, clearly indicates that the IoT will play a major role in the context of 5G. Among the IoT applications, *health* and *medical* are second only to *vehicle*, and well ahead of *industrial environment monitor*, *sensor (things)*, and *robot*.

The second-ranked spectrum discussion is in line with the fact that 5G systems will provide a mix of services for IoT service on different frequencies rather than just the enhanced MBB services like 3G and 4G. The keyword *infrastructure* highlights that the 5G network will be part of infrastructure of the future society and economy. We can also see that human and social factors are clearly relevant. The interconnection of networks also seems to be important. It is interesting that in all the word-clouds, *QoS* and/or *QoE* are mentioned infrequently. Instead, *low latency* and *reliability* appear to be more important performance metrics. These are the new 5G technical challenges.



Fig. 1: Word-cloud analysis of 5G vertical requirements ²

² We merged all the related sections of published white paper on 5G requirements into one document and processed using free online service (www.wordclouds.com). Then, we manually remove the common words (e.g. network, traffic, services etc) and combine synonyms into one word.

It is good to see that the *driver*, who is the end user in this case, is mentioned on a par with *vehicle*, but it is interesting that *patient* and *doctor* are not considered equally in *e-health*. Partially this can be attributed to the fact that car manufacturers, such as BMW, Volvo and Volkswagen, have been involved in 5G research projects such as METIS I and 5GPPP. However, no medical doctors or patient organizations, who are the end users of e-Health and medical applications, are members of any 5G research projects. Their voices are indirectly represented by government officers, *the term citizen is used*. Also *medical* and *e-Health* together claim the second most frequent vertical applications, while the top vertical application is *vehicle*. Looking at other 5G vertical requirements, it is found that most of them are collected by engineers from the telecom operators and vendors by sending questionnaires, with little end-to-end consideration of the vertical products, services, and application environment and context.

These may have new technical requirements and standards impact. For example, form factor, EMC (electromagnetic compatibility) issues and battery power are top concerns for e-Health and wearable devices, which can be attached to the user's skin or weaved into their clothes. The very small form factor is challenging for the implementation of the two receiver chains, where the separation between the antennas of the two receiver chains is so small that the actual radiated performance is close to a single receiver chain. However, except for MTC user equipment, which is for the low data rate market segment, the UE categories defined in current 3GPP specifications are all based on two antennas.

It is also interesting to see how 5G requirements are evolving. The pioneering project METIS first classified five categories of 5G requirements, and nine new usage cases were added at the end of project for future consideration. The Chinese IMT-2000 Promotion Group drew the “blooming flower” to beautify the key capabilities of 5G. The requirement for extreme real-time performance for the tactile Internet was added by NGMN, while 5GPPP further short-listed five vertical fields. Then ITU-T divided the vertical requirements into massive connection and ultra-reliable low-latency connection (URLLC). Recently, 3GPP SA1 took V2X outside URLLC mainly on the grounds that a separate spectrum allocation is needed for V2X. Considering the increasing participation from the verticals, plus the newly available spectrum and developing spectrum policy, the 5G vertical requirements are expected to continue their evolution, at least in the near future.

3. Health 4.0 – virtualization of care

Industrial and emerging economies are undergoing groundbreaking demographic and socio-economic changes. The 19th and 20th century healthcare systems with hospitals and specialists at their core surrounded by General Practitioners are changing in a rapid and progressive manner. More and more people receive treatment in day clinics, day surgery units, doctors' surgeries, at home – or over the Internet. The delivery of care in the future will be distributed and patient centered rather than hospital based and practitioner focused. So far this trend has only been

visible by studying statistics on hospital beds, treatment costs, doctor numbers, demographics and case mixes³.

However, there is growing evidence for a significant shift towards virtualization and individualization of care⁴. The emergence of new telecommunication technologies, such as Long term Evolution (LTE) technology and the 5th Generation Network (5G) are having a significant impact on the strategy development of healthcare systems and their providers. According to the UK National Information Board latest mobile phone technologies should be used to enable and empower lesser qualified carers (informal carers) to adopt routine tasks which otherwise would have to be conducted by professionals, thus making use of individual social capital⁵. Pharmaceutical companies are conducting research into smart pharmaceuticals aiming to collect real-time information from patients in order to massively enhance the effectiveness and the efficiency of their products. Examples include smart asthma inhalers, insulin pens and smart wound dressings. Manufacturers of medical devices such as infusion pumps, monitors, ventilators and hospital beds are looking for strategies to hyper-connect these machines to integrate patients and professionals.

Overall, manufacturers in the medical domain are seeking to transform their products into real time services, which then on the basis of new or amended business models can be integrated and aggregated according individual requirements and preference. This sits perfectly well with recently launched concepts such as Precision Medicine (US) or Individualized Medicine (Europe)⁶. So far these plans and visions have not been sufficiently supported by existing network technologies.

Although 4G networks are superior to 3G networks connectivity is limited to the operating frequency of the smart phone, which has in the past frequently been seen as the major gateway for accessories. The classical examples are the fit bit or different types of smart watches, which are able to collect some biological parameters and store them on a local or distributed platform. However, the strong growth of the Internet of Things and the trend towards a hyperconnected world has made the use of the smartphone as a universal gateway almost obsolete ⁷. Technologies such as Narrow Band IoT (NB IoT) or LoRa are new Radio Access Technologies utilizing alternative frequencies to enable “Things” in a medical universe. These technologies, which empower sensors to allow the connection of the physical world (biological system) and the virtual world (platform) are likely to become components of what is about to become 5G. However, these cyber-

³ Fricker SA, Thuemmler C, Gavras A (Editors) (2015) Requirements Engineering for Digital Health, Springer

⁴ Dorsay ER, Topol EJ (2016) State of Telehealth, N Engl J Med 2016; 375: 154-161

⁵ UK National Information Board (2014), Personalized health and Care 2020 HM Government, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/384650/NIB_Report.pdf

⁶ CF Collins FS, Varmus H (2015) A New Initiative on Precision Medicine, N Engl J Med 2015;372:793-795

⁷ Vermesan O, Friess P (Editors) (2015) Building the Hyperconnected Society, River Publishers

physical systems are the very essence of what has been discussed as a major trend in industrialization over recent years, namely industry 4.0⁸. Industry 4.0 design principles have recently been investigated and confirmed for the automotive industry in a study by the AUDI Foundation Chair Supply Net Order Management⁹.

The authors could identify and distinguish five design principles: Interoperability, Virtualization, Decentralization, Real-Time Capability and Service orientation. Currently investigations are under way to confirm these principles for the health domain. First results suggest that the design principles identified by Herrmann et al also apply to the health domain, hence why it seems justified to conclude that the expression Health 4.0 corresponds to the technical term of industry 4.0. Health 4.0 will support the collection of data in the real world and their transformation and aggregation into more complex services (virtual world). This will allow for delivery of care close to the patient's domain (hospital to home) (Virtualization and decentralization). The delivery of (virtualized) care will be in real time and based on (next to) real time data collection. There is a strong trend to organize care in services which can be delivered anywhere, any how and at any time, rather than for patients having to move physically to hospitals or doctor's surgery or having healthcare professionals to perform tasks in the patients home which could have equally been performed by a member of the patient's social network. Health 4.0 may provide strategies to enable pharmaceutical companies and manufacturers of devices to take on extended responsibilities by transforming their roles from those of a manufacturer into one of a service provider. This would offer patients, professionals and carers more choice but would also require new business models. From an information communication technology perspective reliable and predictive levels of end-to-end quality of service (QoS) are needed which need to be carefully weighed against the notion of net neutrality¹⁰.

Simply put Health 4.0, with 5G as its foundation, will see well-being, social care, and healthcare services transition from supplier-led to person-led. There are several important concepts in this seemingly simple statement – the inclusion of well-being in the care spectrum, the transition of leadership of services, and use of the term 'person' not 'patient'.

5G provides a technical foundation for much opportunity in health domain. In parallel to the formal health and social care services, 5G enables the consumer market to play a role. Consumer devices have proliferated in the marketplace. These devices cover the range of data-generating apps through fit bit-like devices that

⁸ acatech, National Academy of Science and Engineering (2013), Recommendations for implementing the strategic initiative INDUSTRIE 4.0,
http://www.acatech.de/fileadmin/user_upload/Baumstruktur_nach_Website/Acatech/root/de/Material_fuer_Sonderseiten/Industrie_4.0/Final_report__Industrie_4.0_accessible.pdf

⁹ Herrmann M, Pentek T, Otto B (2015) Design Principles for Industrie 4.0 Scenarios, Audi Stiftungslehrstuhl SupplyNet Order Management

¹⁰ BEREC (2016) Draft BEREC Guidelines on implementation by National Regulators of European net neutrality rules, BEREC Document Number BoR (16) 94,
http://berec.europa.eu/eng/document_register/subject_matter/berec/public_consultations/6075-draft-berec-guidelines-on-implementation-by-national-regulators-of-european-net-neutrality-rules

automatically collect and share data, through what would otherwise be considered devices solely in the purview of the medical community like pulse oximeters, which measures oxygen saturation in a person's blood non-invasively. This availability and proliferation of consumer devices is pushing healthcare from treatment triggered by symptoms and medical incidents to more self-diagnosis and care, and health. With a wealth of devices and hence knowledge, the average person is able to make different choices to proactively impact health and well-being and thus healthcare truly now includes well-being. As care includes well-being more and more, the term patient will no longer apply. A patient by definition is someone seeking healthcare; someone that already has health symptoms or experienced an incident. With consumer devices and virtualized 'care', the patient becomes less relevant and the person more relevant.

This will also trigger discussions around new business models, which are able to integrate well-being, health and social care approaches. This might lead to individualized healthcare accounts, which may enhance people's ability to design their individual care profile that might be funded from different sources.

It is easy enough to visualize people using IoT technology and consumer devices for their well-being to monitor and manage exercise, sleep, heart rate and so on. Consumer-oriented medical devices will extend this, allowing people to more easily manage their chronic conditions in ways that only their health care providers could formerly. Proper management of chronic disease leads to better patient outcomes. Chronic obstructive pulmonary disorder (COPD) is a good example. Better disease management is ensuring that people not only take exercise and their medications and refrain from smoking, but that also ensuring that intervention is having the right impact and can be escalated if needed. This can be achieved through the provision of 'Things' and automated, intelligent use of the data created, shifting treatment from formal institutions and providers to people. As these devices become more and more commonplace health care professionals will be able to work based less on demand and more on need, thus systemically increasing the efficiency of health care systems. It is already accepted that approximately 15% of people attending A&E departments in England could have been treated in the community¹¹. On the other hand there are serious concerns about systemic overtreatment¹² this changed model does not come without its challenges. Most obviously, as noted in the design principles for Industry 4.0, there is the need to interoperate technically and to do so securely, protecting people's privacy. In addition, defining the standard by which to exchange the data in health is not enough to successfully interoperate. What each player means by the data, and under what exact circumstances varies widely within the health system. Standards will need to extend to a common dictionary among players, however easier this may become with data collection in real time. Two real

¹¹ The King's Fund (2016) What's going on in A&E, <http://www.kingsfund.org.uk/projects/urgent-emergency-care/urgent-and-emergency-care-mythbusters#increased>

¹² Moynihan R, Doust J, Henry D (2012), Preventing overdiagnosis: how to stop harming the healthy, BMJ2012; 344:e3502 doi: 10.1136/bmj.e3502

challenges with Health 4.0 will be the plethora of available data and the loss of control of 'care'.

One of the key challenges of Health 4.0 is to integrate, aggregate and ultimately "make sense" of an exponentially growing amount of available individual data from a variety of sensors and smart devices. The developments under Health 4.0 however do require health care providers to adopt new roles, namely to develop levers of control and establish governance to prevent the unlawful distribution of patient data on the interface between medicine and information communication technology.

However, current infrastructures and strategies have to evolve to allow for more degrees of freedom and the empowerment of people with regards to the management of their own health. This might require some investment but ultimately, there is no alternative if the quality of care and the quality of experience in health care is to be maintained.

The key take-aways can be summarized as follows:

- Healthcare models are rapidly changing due to demographic and socio-economic changes from a hospital based, specialist focused approach to a distributed patient centric care model
- The point of care is shifting from hospitals towards GP surgeries, day-clinics, care homes, patients' own homes and the Internet
- The empowerment of patients and their formal and informal carers has become a prime target of health care strategy development in Europe and elsewhere
- Emerging new network technologies, including 5G, will form the backbone of future healthcare, enabling the Internet of Things, Smart Pharmaceuticals and Individualized Medicine
- Cloud computing, Big Data and enhanced security will enable virtualization and individualization of care and allow the application of Industry 4.0 design principles in health care (Health 4.0).

4. Network infrastructure

4.1 5G requirements/identify architectural trends

As discussed earlier, 5G is a key enabling technology for the Internet of Things. Therefore IoT features strongly in the attempt to decide the requirements for these networks. After scrolling through the current literature and standards documentation, requirements can be divided into two categories:

1. User-driven requirements in terms of QoE, QoS, user satisfaction and speed of the connection. These are a few user-driven requirements:

- Data rate and latency per user
 - The performance perceived by the user in terms of capacity and latency
 - QoR (Quality of Resilience)
 - The ability to react to failures, such as link cuts or software errors, automatically by redirecting traffic from routes affected by failures to routes which are fault-free, resulting in the user's perception of continuous service.
 - User Mobility
 - The provision of continuous service to the user despite the movement of the user and how their location, velocity and acceleration change over time. This is usually represented by mobility models for various conditions, environments and services.
 - Context Awareness and Management
 - This is complementary to the other requirements, and represents an application's ability to adapt to changing circumstances and respond according to the context of use. Definitions of models and architectures able to support such applications are still an area of active research and consensus has not been reached. This is of particular importance for the health care domain.
2. Network-driven requirements in terms of network operation and management. These could be:
- Scalability
 - Capacity
 - Cost
 - Energy efficiency
 - Security and Privacy
 - Coverage
 - Network flexibility
 - Spectrum management

4.2 Technology options capabilities and drawbacks

User devices in an e/m-Health network include implanted sensors, wearables, and portable devices, which together cover a wide frequency spectrum range: from 5-50MHz for implanted devices¹³ all the way to the mm-Wave frequency band for 5G portable devices. Various devices, services, and applications envisioned in e/m-Health also lead to a wide range of requirements in communication and computation. For example, the ability to easily densify and scale the network with a large number of connected sensors and wearables is the most essential task for the wireless body area network (WBAN) in a home environment. On the other hand, coverage is the top-one consideration in a longer range wireless local area network (WLAN) to connect patients, relatives, doctors to the remote server and data center. To meet the diverse requirements of different applications and use case scenarios, the following requirements need to be achieved in the system:

¹³ 802.15.6 IEEE Standard for Wireless Body Area Networks.

- Flexibility: the system can flexibly support the various requirements, for example, reliability, latency, spectrum efficiency, energy efficiency, device form factor and cost
- Scalability: the system can be scaled to support new deployment scenarios and use cases
- Security: the system needs to ensure secure operation

On the infrastructure network side, dedicated protocols and hardware might be used to support each of the application scenarios, which often require long deployment time and high cost. A more cost-efficient way would be to support the various application scenarios in a common platform, which allows time- and cost-efficient configuration to support the various application scenarios. To this end, technologies such as network function virtualization (NFV) and software-defined networks (SDN) can be applied. NFV virtualizes the physical network resources build on which SDN realizes the dynamic configuration of control-plane and user-plane for each of the applications. Virtualization techniques to flexibly, support the different applications, have been primarily applied in the core network. With time we see this trend to continue and expend into the radio access networks and the air interface.

On the device side, while the wearable e/m-Health devices may need to be in small form factor, the requirements on computation and processing can be high. Moreover, with a massive number of devices with sensing capability being deployed, the amount of data to be transmitted from the devices to the cloud can be high, which impose high traffic demand on the radio network. To address these challenges, edge cloud and edge computation should be supported to process data locally. This will allow low latency processing for critical m-Health applications, constrain traffic in the local network at the edge, reduce the traffic load in the deeper radio network and offload the computation load from small m/e-Health devices to the edge server. Moreover, edge clouds reduce the amount of information propagation in the network, which enhances privacy and security of patients' medical data.

Health status and medical data can be extreme sensitive personal information. Security is a key requirement for e/m-Health services. On the other hand, the employment of stringent security mechanisms can result in additional latency being introduced. The system design needs to balance latency and security. Different security mechanisms with different levels of protection can be applied to meet the various communication and security requirements of the e/m-Health applications.

One requirement, which has not been fully developed in the 5G is on time synchronization. Typical medical sensors sample signals from different positions of the body sequentially, e.g. EEG, EMG and others. Figure 2 shows another example for gait analysis. The parameters gathered by multiple sensors need to be synchronized to reflect the value of the different physiological parameters at the same time. This is particularly true if the medical sensors work in the licensed-exempt spectrum, which could be lossy and noisy. The arrival sequence of sensing data is not the same as the sequence of data sampling time. Another case is that a patient may use multiple medical devices at the same time, time synchronization among them is needed too. The accuracy of time synchronization depends on the

sample rate of medical sensor. It could vary from microsecond to millisecond. Meanwhile, the time synchronization must be low power consumption.

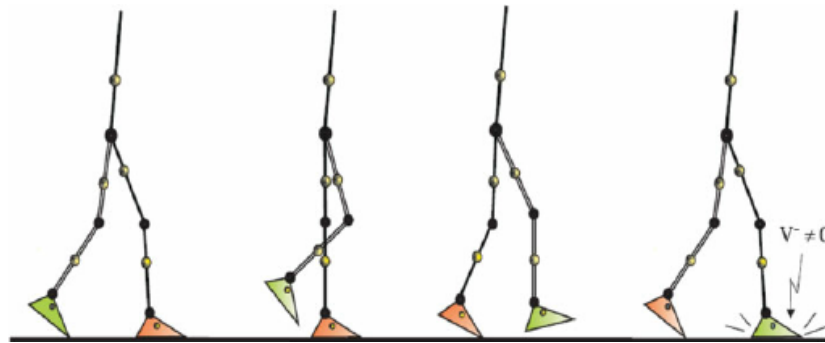


Fig. 2: Walking gait illustration

Data access governance in 5G¹⁴

The old paradigm of data and metadata being collected and stored en masse without a clear supervision are long gone – governmental agencies have firmly established their position that collection, processing, and storage of data (such as personal data) is to be governed by rules and regulations of the legal system. This is reflected for example in legal acts such as the European Commission’s Directive 95/46/EC (*Data Protection Directive*), and Directive 2002/58/EC (*e-Privacy Directive*), which denote that (1) *any information*, which is (2) *relating to* (3) *an identified or identifiable* (4) *natural person* is personal data and as such subject to regulations of law [1].

The implications of regulatory intervention are manifold. The first thing to keep in mind is the distinction between the *data subject* (the individual the data is about),

¹⁴

1. Data Protection Working Party, ‘Opinion 4/2007 on the concept of personal data’. 20-Jun-2007.
2. A. Paulin and T. Welzer, ‘A Universal System for Fair Non-Repudiable Certified e-Mail without a Trusted Third Party’, *Computers & Security*, 2013.
3. S. Kremer, O. Markowitch, and J. Zhou, ‘An intensive survey of fair non-repudiation protocols’, *Computer Communications*, vol. 25, no. 17, pp. 1606–1621, Nov. 2002.
4. A. Paulin, ‘Through Liquid Democracy to Sustainable Non-Bureaucratic Government - Harnessing the Power of ICTs for a novel form of Digital Government’, *JeDEM*, vol. 6, no. 2, 2014.
5. A. Paulin, ‘Towards Self-Service Government - A Study on the Computability of Legal Eligibilities’, *Journal of Universal Computer Science*, vol. no. 12, pp. 1761–1791, Jun. 2013.
6. A. Paulin, ‘Informing Smart Cities Governance? Let Us First Understand the Atoms!’, *Journal of the Knowledge Economy*, Apr. 2016.
7. E. Bertino, G. Ghinita, and A. Kamra, *Access control for databases concepts and systems*. Boston: Now, 2011.
8. S. Chaudhuri, T. Dutta, and S. Sudarshan, ‘Fine Grained Authorization Through Predicated Grants’, 2007, pp. 1174–1183.

who is the owner of the data, and the *data controller*, which is the organization that stores or processes the data, without owning it. This implies that the *data subject* must have (regulated) control over its data, has the right to rectify or retract it, and must be able to control how the data is shared. To supervise the movement of data along the value chains, *fair non-repudiation*, which produces non-repudiable proof of data or message transfer between two parties (cf. [2], [3]) must be deployed to prevent loss of control over the movement of data.

Law however is dynamic and itself subject to frequent changes, caused by legislative or judicative intervention. Any future change in regulation causes discomfort and additional expenditure, as it requires *data controllers* to implement new policies, establish new governance bodies, make new investments – all of which are stifling the swift and efficient implementation of new regulative policies. To overcome this, research from the e-Governance and Smart City domains introduced *constellation based reasoning* [4]–[6], which utilizes *dynamic fine-grained access control* [5]–[8] to enable legislative bodies to centrally control access policies of distributed data bases [4]. These technologies enable governance bodies to dynamically regulate which stakeholders will under which conditions have access to data, without causing disruptions at the side of the *data controllers*. This will give full flexibility to regulate area such as freedom of information access, access by law enforcement agencies, by researchers, by government bodies, by *data subjects* themselves, by service providers (such as caregivers) and so on.

4.3 5G for e/m-Health

Figure 3 shows the overall structure of an m-health network based on a medical health cloud computing platform and the platform service mode. Some public wireless networks (Bluetooth wireless PAN, Wi-Fi, 4G cellular network and NB-IOT) are used to offer wireless medical services. In the home or hospital environment, wearable or portable devices and IP-based terminals complete the data collection and transmission. This data, after reasonable user authorization, can be accessed by the user themselves or their relatives at anytime and anywhere. The new health management system combines the Internet of things (IoT) with cloud computing and big data technology, to fully exploit health status change information. Through data mining, feature extraction and data analysis, the potential disease can be screened and alarmed in advance, based on the medical and health data collected by various IOT terminals in hospital and home environments. Targeted preventative intervention can block, delay or even reverse the developing disease.

In the family scenario, by means of monitoring wearable devices, E-health Management (EHM) customers can sample their own physiological parameters at any time, and send them to health-care institutions in a timely and accurate way. The staff of health-care institutions can provide guidance to EHM customers based on both the past and current data received regarding their conditions. The sampled physiological parameters can be transmitted by cellular network (5G or NB-IOT) or Wi-Fi. In the family scenario, m-health monitoring wearable devices should have the basic medical monitoring capabilities, as well as the features of miniaturization, portability, easy operation and the capability of short-distance communication.

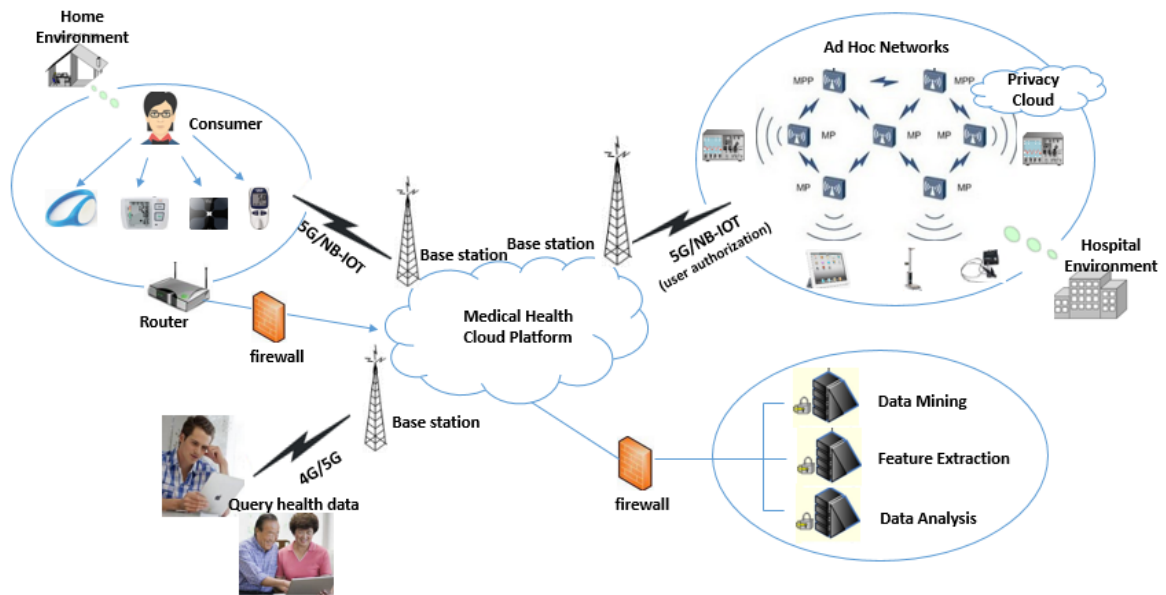


Fig.3: Network Architecture of m-Health

In the hospital scenario, an Ad-Hoc Network is established to realize a self-building, self-diagnosing, self-healing and self-routing network, which reduces user participation and improves the efficiency of networking. Many monitoring terminals or diagnosis instruments gather data and save data in the privacy cloud within the hospital. The data, after reasonable user authorization, can also be sent to the public medical and health cloud server by wireless interface such as 4G/5G and NB-IOT, which can be further queried by patients and their relatives anywhere for healthcare purposes.

Other scenarios such as the disaster rescue scenario and the pre-hospital emergency scenario, can be realized using m-health technology. In the disaster scenario, by means of advanced wearable diagnostic devices, the sampled physiological parameters of injured people can be obtained at anytime, anywhere by the doctors located both inside and outside of the disaster area. The pre-hospital emergency scenario is usually offered outside the hospitals. It can be defined as an emergency medical treatment for patients injured by accidents or life-threatening diseases, and who are treated during transport from an on-site location to the hospital, which can reduce the time and costs of patient transportation. A remote medical treatment-assistant system makes it possible for patients in an ambulance who require specialist medical care to have face-to-face consultations with doctors in the hospital. In other words, it enables the emergency medical staff to send medical data (including sounds, images and video), captured using wearable medical devices, to the hospital.

Usage case	Coverage	Download data rate	Upload data rate	Mobility	Reliability	Latency	Battery lifetime
Home	Short/Wide	<2Mbps (Home monitoring); <25Mbps(e.g. remote diagnosis)	<2Mbps(Ho me monitoring); <25Mbps(e. g. remote diagnosis)	~1m/s	99.99%	10-100ms	Weeks
Hospital	Short/Wide	<25Mbps	<25Mbps	~1m/s	99.99%	10-100ms	Days
Disaster	Wide	<25Mbps; <200Mbps (e.g. remote surgery based on VR/AR)	<25Mbps	<10m/s	99.99%	<10ms	Days
Pre-hospital Emergency	Wide	<25Mbps	<25Mbps	<500k m/h	99.99%	<10ms	Days

Table II: Healthcare scenarios. (Prof, Kang, BUPT)

5. Application Scenarios

5.1 Use Case 1: Multiple Sclerosis

Multiple sclerosis (MS) is a representative inflammatory demyelinating disease of the central nervous system (CNS). Both genetic predisposition and environmental factors are essential for the development of MS. It is estimated that more than 2.3 million people affected. Importantly enough, MS is one of the world's most common neurological disorders and a major cause of non-traumatic disability among young adults in many countries¹⁵.

MS exhibits a variety of symptoms, though some of them are typical particularly at the initial stages of the disease. They may result from involvement of sensory,

¹⁵ Atlas of MS 2013. Mapping multiple sclerosis around the world. MSIF, 2013, pp. 1–28.

motor, visual, and brainstem pathways. The majority of patients with MS initially present with relapsing remitting episodes of new or recurrent neurological symptoms¹⁶.

In general, there are standardized definitions for four MS clinical course phenotypes: relapsing remitting (RR), secondary progressive (SP), primary progressive (PP), and progressive relapsing (PR)¹⁷ with some recent modifications¹⁸. The first clinical event suggestive of demyelination though not yet of MS is termed clinically isolated syndrome (CIS) and can be optic neuritis, incomplete myelitis, or brainstem syndrome¹⁹. About two-thirds of these patients develop clinically definite MS (CDMS)²⁰.

The McDonald criteria are used for MS diagnosis. They incorporate clinical and/or MRI data for the identification of dissemination in time (DIT) and space²¹. However, a number of other diseases need to be differentially diagnosed²².

The underlying pathology is rather variable, similarly to the clinical profile of the disease and is currently considered a primarily autoimmune disorder of the CNS characterized by focal lymphocytic infiltration and demyelination²³ and one of the main causes of non-traumatic neurological disability in young adults. However, diffuse axonal and neuronal degeneration is evident although early in the disease process^{24 24 25 26 27}, the Wallerian degeneration (WD) being a major component of

¹⁶ Garg N, Smith TW. An update on immunopathogenesis, diagnosis, and treatment of multiple sclerosis. *Brain Behav.* 2015; 5(9):e00362.

¹⁷ Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis: results of an international survey. *Neurology* 1996; 46:907–911.

¹⁸ Lublin FD, Reingold SC, Cohen JA, Cutter GR, Sørensen PS, Thompson AJ, Wolinsky JS, Balcer LJ, Banwell B, Barkhof F, Bebo B Jr, Calabresi PA, Clanet M, Comi G, Fox RJ, Freedman MS, Goodman AD, Inglesse M, Kappos L, Kieseier BC, Lincoln JA, Lubetzki C, Miller AE, Montalban X, O'Connor PW, Petkau J, Pozzilli C, Rudick RA, Sormani MP, Stüve O, Waubant E, Polman CH. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology.* 2014; 83(3):278-86.

¹⁹ Miller, D., F. Barkhof, X. Montalban, A. Thompson, and M. Filippi. 2005. Clinically isolated syndromes suggestive of multiple sclerosis, part I: natural history, pathogenesis, diagnosis, and prognosis. *Lancet Neurol.* 4:281–288.

²⁰ Fisniku LK, Brex PA, Altmann DR, et al. Disability and T2 MRI lesions: A 20-year follow-up of patients with relapse onset of multiple sclerosis. *Brain* 2008a; 131: 808–817.

²¹ Polman, C. H., S. C. Reingold, B. Banwell, M. Clanet, J. A. Cohen, M. Filippi, et al. 2011. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann. Neurol.* 69:292–302.

²² Garg N, Smith TW. An update on immunopathogenesis, diagnosis, and treatment of multiple sclerosis. *Brain Behav.* 2015;5(9):e00362.

²³ Compston, A., Coles, A., 2008. Multiple sclerosis. *Lancet* 372 (9648), 1502–1517.

²⁴ Di Filippo, M., Anderson, V.M., Altmann, D.R., Swanton, J.K., Plant, G.T., Thompson, A.J., Miller, D.H., 2010a. Brain atrophy and lesion load measures over 1 year relate to clinical status after 6 years in patients with clinically isolated syndromes. *J. Neurol. Neurosurg. Psychiatry* 81 (2), 204–208.

²⁵ Dutta, R., Trapp, B.D., 2011. Mechanisms of neuronal dysfunction and degeneration in multiple sclerosis. *Prog. Neurobiol.* 93 (1), 1–12.

²⁶ Trapp, B.D., Peterson, J., Ransohoff, R.M., Rudick, R., Mörk, S., Bö, L., 1998. Axonal transection in the lesions of multiple sclerosis. *N. Engl. J. Med.* 338 (5), 278–285.

axonal pathology²⁸. In particular, neuroaxonal damage accumulates with disease progression and it is thought to be the major cause of neurological disability in the long term²⁹.

During the last years several mechanisms potentially underlying neuronal damage in MS have been hypothesized²⁶. There is increasing evidence for a potential energy metabolism failure leading to neuroaxonal death³⁰ since mitochondrial defects have been demonstrated during the course of the disease³¹⁻³², despite increased mitochondrial content³³⁻³⁴. These defects could, at least in part, explain the hypoxia-like tissue injury seen in MS lesions. Indeed, reactive oxygen species (ROS) and nitric oxide (NO) produced by activated microglia may impair mitochondrial function³⁵ and thus may link microglial activation in MS lesions with a hypoxia-like tissue injury³².

Impact of the disease

Given the variety of symptoms and clinical course together with the unpredictable and progressive character of the disease, MS has a profound and life-long impact on patient's quality of life (QoL) affecting not only physical, (visual and cognitive function), but also psychological and social aspects right from the moment of diagnosis³⁶⁻³⁷. Moreover, it is estimated that as early as (on average) three years after diagnosis, unemployment is a major issue for as many as half of the MS

²⁷ Grigoriadis N, Ben-Hur T, Karussis D, Milonas I. Axonal damage in multiple sclerosis: a complex issue in a complex disease. *Clin Neurol Neurosurg*. 2004 Jun;106(3):211-7.

²⁸ Dzedzic T1, Metz I, Dallenga T, König FB, Müller S, Stadelmann C, Brück W. Wallerian degeneration: a major component of early axonal pathology in multiple sclerosis. *Brain Pathol*. 2010;20(5):976-85.

²⁹ Fisniku, L.K., Chard, D.T., Jackson, J.S., Anderson, V.M., Altmann, D.R., Miszkiet, K.A., Thompson, A.J., Miller, D.H., 2008b. Gray matter atrophy is related to long-term disability in multiple sclerosis. *Ann. Neurol*. 64 (3), 247–254.

³⁰ Trapp, B.D., Stys, P.K., 2009. Virtual hypoxia and chronic necrosis of demyelinated axons in multiple sclerosis. *Lancet Neurol*. 8 (3), 280–291.

³¹ Mahad, D., Ziabreva, I., Lassmann, H., Turnbull, D., 2008. Mitochondrial defects in acute multiple sclerosis lesions. *Brain* 131 (Pt 7), 1722–1735.

³² van Horssen, J., Witte, M.E., Ciccarelli, O., 2012. The role of mitochondria in axonal degeneration and tissue repair in MS. *Mult. Scler*. 18 (8), 1058–1067.

³³ Blokhin A, Vyshkina T, Komoly S, Kalman B. Variations in mitochondrial DNA copy numbers in MS brains. *J Mol Neurosci* 2008; 35:283–287.

³⁴ Witte, M.E., Geurts, J.J., de Vries, H.E., van der Valk, P., van Horssen, J., 2010. Mitochondrial dysfunction: a potential link between neuroinflammation and neurodegeneration? *Mitochondrion* 10 (5), 411–418.

³⁵ Bolanos JP, Almeida A, Stewart V, Peuchen S, Land JM, Clark JB, et al. Nitric oxide-mediated mitochondrial damage in the brain: mechanisms and implications for neurodegenerative diseases. *J Neurochem* 1997; 68: 2227–40.

³⁶ Pugliatti M, Rosati G, Carton H, et al. The epidemiology of multiple sclerosis in Europe. *Eur J Neurol* 2006; 13: 700–722.

³⁷ Zwibel HL and Smrtka J. Improving quality of life in multiple sclerosis: An unmet need. *Am J Manag Care* 2011; 17(Suppl. 5): S139–S145.

patients, who may therefore depend on a disability pension or on their family and friends for the rest of their life³⁸. Consequently, it is evident that MS exhibits a high burden for patients, their caregivers – family members and society as a whole.

The aim of treatment

There is currently no cure for MS. However, much progress has been performed during the last in the management of disease activity and progression through specialized care. The early diagnosis and the establishment of patient-centered therapeutic strategies together with the use of appropriate medication such as disease-modifying drugs (DMDs) and symptomatic therapies have largely contributed to a better outcome of MS patients.

The therapeutic armamentarium of DMDs includes five interferon formulations, two versions of glatiramer acetate, mitoxantrone, natalizumab, fingolimod, teriflunomide, dimethyl fumarate, and alemtuzumab. After a disease-modifying therapy is chosen, vigilance for clinical or radiographic breakthrough disease is very important, as this may suggest a suboptimal response to the chosen therapy. Furthermore, symptom management and wellness should always remain part of overall therapeutic strategy³⁹. Last but not least, pharmacovigilance and close monitoring for potential side effects and potentially harmful iatrogenic complications are of great importance in the overall management of MS.

Our aim is to control the disease activity, in particular the reduction of the annual relapse rate and the ongoing disability progression. To this aim, an early initiation of treatment at the early stages of the disease is of great importance for a better outcome for the patient. It is of importance to keep in mind that there is usually a latent period from the time when pathology initiates until the clinical expression either as a relapse or as progression. Consequently, using clinical and/or laboratory criteria we need to anticipate the potential of future disease activity and make appropriate adaptations in treatment. All DMDs have the potential to provide a long-term control of disease activity. It remains to determine which DMD may be the most appropriate one on an individual basis.

Problems in care and management of the disease and the potential role of 5G networks

The early identification and evaluation of symptoms is very important in the disease management. In clinical practice, it has been noticed that patients may underestimate a particular change in their neurological function until it becomes particularly evident. Moreover, patients may not be able to determine precisely during their follow-up the initiation of any impairment they may have had. This impaired provision of accurate information may be attributed to concomitant

³⁸ Gold R, Toumi M, Meesen B, Fogarty E. The payer's perspective: What is the burden of MS and how should the patient's perspective be integrated in health technology assessment conducted for taking decisions on access to care and treatment? *Mult Scler*. 2016;22(2 Suppl):60-70.

³⁹ Jones DE. Early Relapsing Multiple Sclerosis. *Continuum (Minneapolis, Minn)*. 2016;22(3, Multiple Sclerosis and Other Demyelinating Diseases):744-760.

cognitive impairment and/or memory disturbance⁴⁰. Therefore, a loss of information about their recent medical history in between the follow up time points may lead to an overall impaired clinical evaluation of the disease burden.

A good example of an early identification of functional impairment in MS is the walking ability of the patients characterized by decreased walking endurance and confidence and falls⁴¹. Walking impairment is one of the most noticeable and serious manifestations of MS, usually occurring early during MS. Walking disturbances have been reported to have the greatest impact on socioeconomic outcomes occurring during the early stages of disability. In Europe, only half of the MS patients with an Expanded Disability Status Scale 3 (EDSS 3; fully ambulatory patients) are employed and this is further decreasing to 20% of patients with an EDSS 6 (patients needing a walking aid)⁴². Interestingly enough, the affected individual prior to relevant clinical manifestation often perceives walking impairment. It would therefore be important that the patient would be able to provide such a notice in real time and not after a period of time until the scheduled appointment with the doctor. Patient perceptions should lead to pre-emptive management strategies to maintain independence and delay as long as possible the need for walking assistive devices or caregiving.

Moreover, time is an important factor and any delay of the appropriate identification and management of the symptoms may ultimately lead to a more permanent functional impairment. Evidently, when used in tandem, patient-reported measures in real time and objective evaluation by the physicians either concomitantly or during scheduled appointments, can help monitor changes and facilitate patient-clinician discussions of problems, management strategies, and long-term goals related to walking impairment⁴³. Further, due to the various factors interfering with symptom appearance or severity throughout a time period (concomitant infections, environmental conditions such as temperature and humidity) it may very well be that the evaluation of the patient during a scheduled follow-up may not correspond to the burden of this particular symptom on a daily basis. It has recently been reported that using in-home sensors to analyze gait parameters in real time is feasible and could lead to better analysis of gait in persons with MS⁴⁴. Moreover, internet-guided

⁴⁰ Pflugshaupt T, Geisseler O, Nyffeler T, Linnebank M. Cognitive Impairment in Multiple Sclerosis: Clinical Manifestation, Neuroimaging Correlates, and Treatment. *Semin Neurol.* 2016;36(2):203-11.

⁴¹ Cameron MH and Nilsagård YE. Measurement and treatment of imbalance and fall risk in multiple sclerosis using the international classification of functioning, disability and health model. *Phys Med Rehabil Clin N Am* 2013; 24: 337–354.

⁴² Kobelt G, Berg J, Lindgren P, et al. Costs and quality of life of patients with multiple sclerosis in Europe. *J Neurol Neurosurg Psychiatry* 2006; 77: 918–926.

⁴³ Smrtka J1, Brown T2, Bjorklund G3. Loss of mobility and the patient burden of multiple sclerosis: expert opinion on relevance to daily clinical practice. *Postgrad Med.* 2016;128(1):145-51.

⁴⁴ Newland P, Wagner JM, Salter A, Thomas FP, Skubic M, Rantz M. Exploring the feasibility and acceptability of sensor monitoring of gait and falls in the homes of persons with multiple sclerosis. *Gait Posture.* 2016; 49:277-282.

interventions can encourage MS patients to implement more physical activity in their lives⁴⁵.

Importantly enough, MS patients may exhibit other symptoms such as fatigue, anxiety, depression, bladder and bowel dysfunctions and sexual problems. These symptoms may either be transient or permanent and their intensity varies throughout the time. Some of these symptoms may also be a sign of a forthcoming relapse or neurological worsening. Again, the notification of these symptoms in real time as well as their record on a daily basis may provide detailed information to the doctors.

Although many tests and scales are available to evaluate the severity or impact of specific symptoms, they are often not used in daily clinical practice. Presumably, time constraints for physicians to perform comprehensive assessments and/or their unfamiliarity with specific metrics of clinically meaningful differences, make interpretation of the relevant evaluations rather difficult. Moreover, not all clinicians may value patient-reported measures as they are potentially biased by mood⁴⁶. However, when the patient perspective is provided in real time, then any impact of concomitant factors may be easily examined thus resulting in a reliable evaluation. Moreover, most of the relevant information would already be available if recorded in real time, thus saving time during patient's scheduled follow-up.

A prerequisite for treatment success with MS, similarly to most chronic diseases, is the regular intake or administration of drugs, that is, a high adherence to therapy⁴⁷. Decreased adherence in MS treatment may increase the relative risk of relapses⁴⁸. MS patients may exhibit variable loss of adherence to treatment due to a number of factors, such as forgetfulness, fear of the injection, lack of efficacy as assessed by the patient, side effects, problems with complex treatment schemes, as well as fatigue⁴⁹. On the other hand, it is very important for the doctor's evaluation of treatment effectiveness to have reliable information about the adherence to treatment. Technology may largely contribute to solve this problem. A good example is the use of an electronic auto-injection device for subcutaneous injection of interferon (IFN) β -1a 44 μ g three times weekly. In a recently published clinical trial it has been reported that the use of this device was associated with high treatment adherence, as objectively assessed using electronic injection logs⁵⁰. Doctors may

⁴⁵ Motl RW, Dlugonski D, Wójcicki TR, et al. Internet intervention for increasing physical activity in persons with multiple sclerosis. *Mult Scler* 2011; 17: 116–128.

⁴⁶ Feys P, Giovannoni G, Dijsselbloem N, Centonze D, Eelen P, Lykke Andersen S. The importance of a multi-disciplinary perspective and patient activation programmes in MS management. *Mult Scler*. 2016;22 (2 suppl): 34-46.

⁴⁷ Osterberg, L. and Blaschke, T. (2005) Adherence to medication. *N Engl J Med* 353: 487–497.

⁴⁸ Ho, P., Bryson, C. and Rumsfeld, J. (2009) Medication adherence. *Circulation* 119: 3028–3035.

⁴⁹ Costello, K., Kennedy, P. and Scanzillo, J. (2008) Recognizing nonadherence in patients with multiple sclerosis and maintaining treatment adherence in the long term. *Medscape J Med* 10: 225.

⁵⁰ Devonshire VA, Feinstein A, Moriarty P. Adherence to interferon β -1a therapy using an electronic self-injector in multiple sclerosis: a multicentre, single-arm, observational, phase IV study. *BMC Res Notes*. 2016;9:148.

also have in real time information via Internet about any missing administration doses.

In order to improve the patient's QoL and reduce the burden on society, MS patients should be comprehensively assessed while being empowered to remain active both in their family and social lives as well as in their work environment. This can be achieved by providing optimal care (rehabilitation, multi-disciplinary assessment and services and so on) and DMDs adapted to the needs of every single patient⁴⁷. In order to better meet the patients' needs, good communication and collaboration between the different stakeholders is essential. This includes MS patients, their caregivers, policy makers, healthcare professionals, researchers, regulators and payers⁵¹. Unfortunately, a wide variation in access to care and treatment exists nowadays across European countries^{47 52} and globally. New technologies allowing e-communication may be of help to facilitate optimal care and (self-) management⁴⁷.

In the new era of MS treatment and on the basis of our current knowledge about MS management, it became pretty clear that the overall therapeutic strategy should always be scheduled on strictly individualized basis. To this end, MS patients should be encouraged to take control over their own disease. They should be educated to record any change in their condition together with any potentially relevant factor they may notice or on the basis of their doctor's advice. The advent of different Internet and mobile applications can support patients in doing so. Mobile technology needs to provide tools in supporting various parameter recording in real time. Relevant clinical studies may further highlight the mobile and Internet technology in MS management. This is an absolute necessity for a variable, fluctuating and largely unpredictable disease such as MS.

5.2 Use Case 2 (Asthma)

Asthma is a chronic respiratory disease with symptoms such as wheezing, shortness of breath, chest tightness, cough, and reversible airflow limitation. Symptoms and airflow limitation both change over time. The prevalence of asthma ranges from 1% to 18% in different countries. Currently, there are about 300 million patients with asthma, and about 30 million in China alone. Each year approximately 25 million people worldwide die from asthma. The cause of death is usually related to poor long-term control and the impact of the last asthma attack, which did not receive timely medical assistance. The large scale epidemiological survey of asthma among children in China in 1990 and 2000 indicated that the prevalence of asthma in children increased by 64.84% in 10 years.

The Internet of Things (IoT) is an important part of a new generation of information technology, which could potentially resolve health care problems. IoT links the

⁵¹ Vermersch P, Faller A, Czarnota-Szałkowska D, Meesen B, Thalheim C. The patient's perspective: How to create awareness for improving access to care and treatment of MS patients? *Mult Scler.* 2016;22(2 Suppl):9-17.

⁵² MS barometer: widespread health inequalities revealed. EMSP, 2014, pp. 1–54.

virtual world to the real world through connections between sensors and working devices. To improve the feasibility of tele-healthcare application in the management of asthma patients, a cloud-based platform, entitled the medical Internet of Things (mIoT), has been established. With mIoT, there is no time and space limitation for physicians and asthma patients to interactively communicate, and asthma patients do not need go to hospital. Instead, they can stay at home or in local community hospitals to perform lung function tests. The core of mIoT is the extension and expansion of the Internet. Cloud computing is crucial to connect various medical sensors such as portable lung function test devices and collect physiological parameters from asthma patients, so that daily surveillance and frequent feedback response between physician and patients are possible. Cloud computing is also important for data processing and data mining. One example is the IBM-developed 'Watson Internet of Things', which is a cognitive system that could learn and provide medical advice to patients. Patients may access the mIoT platform via their mobile terminals to complete an asthma questionnaire at regular intervals, obtain instant and personalized services, or visit medical experts for advice.

The features of mIoT make it suitable to be widely used in the diagnosis and management of asthma, ranging from collecting patient information and medical history, analyzing test results, diagnosing asthma, determining levels of asthma, to individualized treatment of asthma.

Asthma diagnosis. Risk factors for asthma include host factors (genetic factors) and environmental factors. With mIoT, patients could upload their symptoms to the medical center through mobile terminals. After reviewing the medical information, physicians could give medical advice such as performing lung function tests. Patients may perform lung function tests by using portable spirometers and upload the test results to the medical centers. Physicians could then make a decision on whether patients need further tests. In order to improve the management of asthma, a mobile phone-based e-Health app has been developed with five steps, which are:

1. Ask: scan to add patients and to collect consent, questionnaire and personal information
2. Assess: evaluate or analyze examination results including lung function tests or X-ray results
3. Advise: based on the assessment, provide diagnosis, differential diagnosis, and further examination suggestions
4. Arrange: manage patients based on their characteristics, providing patient education, treatment and rehabilitation
5. Assist: based on e-Health, improve the connection between experts and GPs (Figure 4).

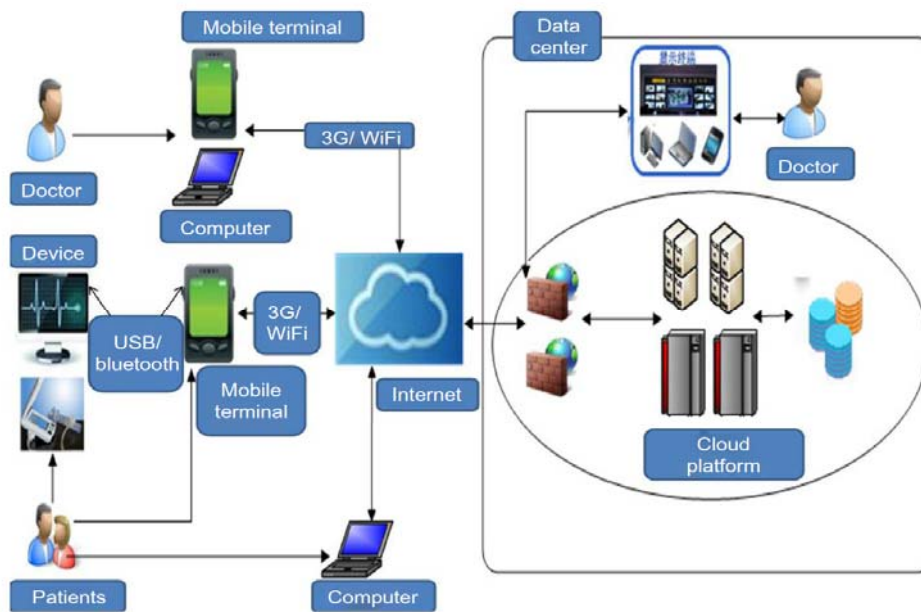


Fig. 4: Serve the patients in home

Based on clinical manifestations, asthma can be classified into:

- acute exacerbation
- chronic persistent and
- clinical remission

Chronic persistent is where patients show on a weekly basis varying degrees of symptoms including wheezing, shortness of breath, chest tightness and coughing. Clinical remission is where symptoms and signs of asthma disappear, lung function returns to pre-attack levels and patients maintain more than three months without any treatment. Physicians can upload the symptoms and signs of asthma patients to the mIoT platform, which can automatically analyze the data and help physicians to determine the levels of asthma.

In 2004, a global survey involving 29 countries showed that only 5% of asthma patients could achieve complete control of standardized treatment. Recent studies demonstrate that about 50% of patients fail to achieve good asthma control in Europe. The reason is mainly because of poor adherence to the treatment of asthma. Lack of knowledge about asthma and lack of receiving proper management are an important cause of asthma aggravation and high mortality.

Following the successful application of mIoT in the management of heart disease and diabetes, it is now being applied in the management of asthma. Asthma education is an important part of asthma management. With mIoT, all kinds of video and audio material related to asthma education can be delivered to the mobile terminals of asthma patients, enabling patients to know more about asthma. In addition, mIoT makes the assessment and monitoring of asthma easier. For example, asthma patients could complete their asthma control tests and asthma

control questionnaires on their mobile phones routinely, so that physicians could monitor the condition of their patients regularly.

5.3 User Acceptance, Regulatory and Ethical Issues

System Evaluation and User Acceptance

The acceptance and success of e/m-Health systems as described in the application scenarios above will depend on the response of all their future users and of all stakeholders involved in the use of the system.

This is achieved by identifying the quality factors that will qualify the system to be used effectively as well as expose the factors that will increase the system's acceptance and usability. It is thus very important to develop and propose an evaluation method in the same time that such systems are proposed and a prototype becomes available to include the technical quality factors together with the user acceptance and usability factors that will enable the early prediction of system quality, effectiveness and success. This method could be based on similar approaches that are successfully used in the healthcare industry and have provided successful predictions in the past. It will have to combine system quality and usability evaluation with user acceptance predictions.

This evaluation method should include the following stages:

- i) The Need for the System
- ii) Technical Quality of the System
- iii) User Satisfaction and Usability Evaluation
- iv) Usefulness
- v) User Acceptance

- i) The Need for System

This is based on a survey that includes the stakeholders and will expose whether such a system is really needed and could successfully improve the performance and effectiveness of the current operating environment.

- ii) Technical Evaluation

This stage will examine the technical quality of the proposed system providing quality assurance on every technical aspect such as source code quality, data quality, system reliability, interoperability, communication aspects, output quality and portability.

- iii) User Satisfaction

User Satisfaction will study the use of the system, covering both input and output. At this stage it is important to predict the usefulness of the input/output and the resistance on the use of the system.

iv) Usefulness

The usefulness of the system will provide an indicator of how useful the system is to the environment that it will operate in terms of performance, structure and processes.

v) User Acceptance

This stage will provide an understanding of why and how health professionals and patients will endorse the proposed system in their every day activities. It will investigate psychological and social issues such as behavior and stress, computer and technology anxiety and workflow.

Regulatory Issues

Healthcare seems to have some resistance to digital transformation. Despite the revolution digital technologies has brought to almost every aspect of our lives and every market segment, the anticipated impact in healthcare has not been seen yet. Patient engagement, connected care, healthy living, independent and active aging have been for long evangelized as an outcome of digital health, but we have not yet witnessed it going mainstream despite the widely produced evidence of the potential. Digital Health is suffering from 'pilotitis' primarily because of these three reasons:

- Healthcare is a highly regulated market and for very good reasons; Uber-like disruption doesn't work in healthcare. This means costly, time consuming procedures that a startup is not ready to endure and venture capitalists are not ready to invest in at least up to now
- Healthcare is a policy driven market, especially in Europe. Consumers are not the decisive group and do not have enough power to push disruption, so technology push de facto disruption is not easy to happen in healthcare, as policy is always slower in adapting than people
- The healthcare value-chain is unique. The usual schema in healthcare is that someone chooses (e.g. the doctor), someone uses (e.g. the patient) and someone pays (e.g. the insurer). Such a schema is rarely – if ever – found in other markets. If B2C does not work then digital technologies find it more difficult to disrupt

Can 5G be a disruptive changer? We think so. Physicians and other healthcare providers have always been the custodians of patient information and data. With the advent of seamless connectivity, smartphones and mobile apps, cloud services and smart connected devices the 5G is bringing patients get an opportunity to take charge of their health and act upon it. Furthermore, they offer individualized health information and an ability to track patient health metrics powered by data analytics - instead of being locked up in Electronic Health Records (EHRs) or not available at all - with unprecedented value, never seen before in such scale and depth. Increased accessibility to this data enables greater transparency, empowers patients and improves overall patient engagement with their healthcare providers.

On the policy front, the US have been pioneers with the ACA (known as Obamacare) and the shift from quantity to quality. 30% of traditional fee-for-service Medicare payments are already tied to accountable care organizations while 50% is the target sought by 2018. The DoHHS also wants to tie 85% of traditional payments to hospitals through value-based or quality-achieving programs by this year and 90% by 2018. The goal is to move away from the old way of doing things, which amounted to, 'the more you do, the more you get paid' by linking nearly all payment to quality and value. As a result accountable care organizations often work together and get rewarded for coordinating care and spending less. Similar suggestions can be found in the recent Green Paper on m-Health published by the EC.⁵³

Ethical Issues

The nature of the data produced by digital health services raises important human subject privacy protection issues. A number of legal and good practice ethics provisions are set in place to cover such issues, which fully cover 5G future services. These include:

- World Health Organization "Handbook for good clinical research practice (GCP)",
- the Helsinki Declaration of 1964 (Recommendation for conduct of clinical research),
- ISO 14155,
- the UNESCO Universal Declaration on Bioethics and Human Rights,
- Regulations EC/46/95, EC/58/2002,
- Directives 95/46/EC and 97/66/EC, about Rights and interest of data subjects,

the recommendations of the European group on ethics in science and new technologies to the European Commission.

Assessing Capacity

High and Doole (1995)⁵⁴ set out a functional approach with the following criteria:

1. ability to understand, comprehend information, and communicate
2. ability to evidence a choice as demonstrated by the presence or absence of a decision
3. ability to make a reasoned choice, including the ability to consider and make judgments about risks and benefits
4. ability to appreciate the circumstances of the decision and the consequences of a decision

⁵³ <https://ec.europa.eu/digital-single-market/en/mhealth>

⁵⁴ High DM % Doole MM. Ethical and legal issues in conducting research involving elderly subjects. Behav Sci Law, 1995; 13(3): 310-335.

5. ability to make a reasonable choice as focused on the outcome of the decision.

Confidentiality

It is important to ensure that confidentiality guidelines should be adhered to at all times. Strictness of regulations differs from country to country. Common practice is to restrict access of participant identifiable data to authorised individuals within the healthcare system. Electronic copies of identifiable data should be encrypted and stored on a password-protected system, within a restricted access area.

Privacy

The EC Green Paper on m-Health consultation showed that people often do not trust m-Health. Having users' consent as well as strong privacy and security tools in place is crucial, as health data is amongst the most sensitive personal data. As a response to that the industry set up a code of conduct. The Code of Conduct⁵⁵ on privacy for mobile health apps has been formally submitted for comments to the Art 29 Data Protection Working Party on June 2016. Once approved by this independent EU advisory group, the Code will be applied in practice: mhealth producers will be able to voluntarily commit to follow its rules, which are based on EU data protection legislation.

6. Delphi Study and Living White Paper

About the Delphi Technique

Delphi is a well-established foresight technique that involves an anonymous polling of the experts or otherwise knowledgeable individuals for their opinions about the future, enabling to allow for judgments about the future to be made democratically, without any one party or expert influencing it. The technique was developed so as to circumvent “follow the leader” tendencies of face-to-face exchanges, and other problems such as the reluctance to discard previously stated opinions (in case of repeated pools being conducted).

Delphi surveys are usually conducted in two rounds. Delphi surveys are most often employed to elicit views as to whether and when particular developments may occur, but the technique can be used for any sort of opinion or information – such as the likelihood and desirability of specific outcomes, impacts of policies or technologies, scenarios and so on. Likewise, Delphi is frequently used with a focus on the dominant views that emerge, but the technique may be oriented more to delineating different points of view. Delphi surveys are often carried out online, and findings are used to prepare policy recommendations, action plans, roadmaps and others.

⁵⁵<https://ec.europa.eu/digital-single-market/en/news/code-conduct-privacy-mhealth-apps-has-been-finalised>

Use of the Delphi Technique

This study aims at eliciting views of experts from different sectors on a wide range of social, economic, political and technological aspects of the 5G and more specifically on e/m-Health over 5G over the next 20 years. Therefore the experts from the technology area (including telecommunication experts), healthcare domain, social/humanistic experts, business experts, as well as experts from law/regulatory/policy sectors were invited to give their opinions on the future developments of 5G, e/m-Health and then 5G for e/m-Health and to provide their views on the likelihood of two healthcare scenarios: for asthma and multiple sclerosis (MS), including advanced options for diagnosis and treatment of these diseases.

The current study contains a set of questions related specifically to technological and otherwise advances like novel radio technologies or novel remote sensing enabling 5G itself (part 1), a set of questions related to technological advances like point of care diagnostics (potentially propelled by 5G) in turn enabling e/m-Health (part 2), and then a set of questions related to other technological advances like Natural Language Processing (potentially propelled by 5G) enabling higher level analytics and personalization features in e/m-Health (part 3). The future 5G-enabled e/m-Health scenarios (asthma and MS) follow (part 4).

This study has been inspired by the past Delphi-method enabled study on Future Internet^{56 57 58}.

⁵⁶ Popper, R. (2010) The Future Internet Delphi: Results of the Delphi Study. Presentation for the Final Workshop of the Towards a Future Internet (TAFI) Project, European Commission. Brussels, 22 November 2010.

⁵⁷ Popper, R. and Forge, S. (2010) Towards a Future Internet: Delphi Survey Round 1 Results. Work package for the Towards a Future Internet (TAFI) Project, European Commission. SMART 2008/0049.

⁵⁸ Popper, R., Blackman, C. and Forge, S. (2010) Towards a Future Internet: Delphi Survey Round 2 Results. Work package for the Towards a Future Internet (TAFI) Project, European Commission. SMART 2008/0049.

Appendix A (Delphi Questionnaire)

In this appendix, we give examples of a set of questions given to our experts as part of the Delphi study.

INSTRUCTION Please answer the questions below. Do not overthink the answers, chose the first answer that feels right.

1 5G technologies & technologies enabling m-Health

Q1.1 When will the 5G become vital for the vast majority of people in ordinary everyday living?

Answers: 2020, 2025, 2030, 2035, beyond 2035, no_answer

2 e/m-Health and 5G

Q2.1 When will the e/m-Health become vital for the vast majority of society in ordinary everyday living?

Answers: 2020, 2025, 2030, 2035, beyond 2035, no_answer

3 5G-enabled Higher Level Analytics and Personalization Features

Q3.1 5G enabled e/m-Health will become much easier-to-use and it will be enabled by increasingly varied, sophisticated and intuitive, real-time ways of interacting with it. When might these interface extensions become widely used?

- Natural language processing (English)
- Natural language processing (other languages)
- Image recognition
- Gesture detection
- Body interface
- Haptic interfaces
- Multi-sensing technologies
- 3D and holographic virtual presence
- Other (specify)

Answers: now, by 2020, by 2025, by 2030, by 2035, beyond 2035, no_answer

4 5G-enabled e/m-Health: Use Cases

Use Case 1: Multiple Sclerosis (MS)

Q4.1 By when is this use case likely to be fulfilled?

Answers: by 2020, by 2025, by 2030, by 2035, beyond 2035, no_answer

5 Tell us about yourself

Age group under 20, 20-30, 30-40, 40-50, 50-60, 60-70, 70-80, 70+

Gender F/M

Region Europe, Africa, Asia, Latin America, North America, Oceania

Specialization technology, health(care), social/humanistic, business,
law/regulatory/policy

Occupation business, education/research, healthcare, government

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c/o Format A AG
Pfingstweidstrasse 102b
CH-8005 Zürich

Secretariat:
Vinod Kumar
e-Mail: vinod.kumar@wwrf.ch
Phone and Fax : +33611181622

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Chairman of the Forum:
Dr. Nigel Jefferies

Editor-in-Chief: Dr. Nigel Jefferies

Contributors

[Pantelis Angelidis](#), "Professor, University of Western Macedonia and President of the Alexander Innovation Zone S.A., Greece"

[Chunxue Bai](#), Professor, Medical Doctor, Respiratory Research Institute Shanghai, Fudan University, China

[Kostas Danas](#), Senior Lecturer of e-Health Systems, Kingston University, London, United Kingdom

[Cindy Fedell](#), Executive Director/CIO, Bradford Teaching Hospitals NHS Foundation Trust, Bradford, UK

[Nikolaos Grigoriadis](#), Professor of Neurology, Medical Doctor, Aristotle University of Thessaloniki and AHEPA Hospital, Greece

[Nigel Jefferies](#), Chairman of the WWRF and Senior Standards Manager, European Research Institute, Huawei Technologies, United Kingdom

[Guixia Kang](#), Professor, Beijing University of Posts and Telecommunications, Beijing, China

[Panayiotis Ketikidis](#), Professor, Vice Principal, South East European Research Centre (SEERC), Thessaloniki, Greece

[Clara Li](#), Senior Research Scientist, Intel, USA

[Christos Politis](#), Professor, Director of Digital Information Research Centre (DIRC) Kingston University, London, United Kingdom

Christoph Thuemmler, Professor, Medical Doctor, Edinburgh Napier University,
Edinburgh, United Kingdom

Katarzyna Wac, Professor, Quality of Life Technologies & mQoL Living Lab, University
of Geneva, Switzerland

Bin Zhen, Wireless Networks Research and Development, Huawei Technologies,
China

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