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AEROAGING – A NEW COLLABORATION BETWEEN LIFE SCIENCES EXPERTS AND AEROSPACE ENGINEERS

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Abstract: An open discussion between experts from life sciences and aeronautics has been held in order to investigate how both area of research overlap and could be relevant to each other, precisely on the topic of aging. Similarities in aging processes and prediction methodologies have been identified between human aging and aircraft aging. Two axis of collaboration have been raised: 1) The identification of the determinants in Aircraft aging (structural aging). 2) The development of P4 Systems medicine inspired new methodologies in the predictive maintenance. .

Key words: Aging, composites, aircraft, life science, health.

Introduction

A workshop was organized in November, 7th, 2016 in Toulouse behalf of the IAGG-GARN and ISAE on AeroAging between experts from both domains (medicine and aeronautics) to identify possible physical or physiological analogies, common processes and developed methodologies to detect and prevent ageing between human and airframe materials. The underlying objective was to investigate in an open discussion between experts how both area of research overlap and could be relevant each other. After reviewing the similarity between aging in life sciences and in aircraft structure, we will review how we can study aging processes in these two areas and finally we will make some propositions on what can be learned and done in practice. Probably P4 Systems medicine can give some opportunities to both maintain functioning human and aircraft performances.

Methods

Participants

A prospective observational study with one-year follow-up using the data of the Utrecht Proactive Frailty Intervention Trial (U-PROFIT). The U-PROFIT trial is a single blind three-armed cluster randomized controlled trial that was conducted in the Netherlands between 2010-2012 (16). This trial evaluated the (cost) effectiveness of a proactive personalized primary care program to preserve daily functioning in older people (n=3092). Details and the results have been described elsewhere (16, 17). Briefly, the first arm consisted of a screening and monitoring intervention based on routine primary care data to identify patients at risk. General practices in this arm we asked to use this instrument and to provide care based on current guidelines. General practices in the second arm received this instrument combined with a nurse-led care program. Registered practices nurses were extensively trained and delivered this evidence-based care program, conducted a comprehensive geriatric assessment at home, developed a care plan in close collaboration with the GP and other health care professionals (17). General practices in the third arm provided care as usual.

In the current study, data was used of participants enrolled in the control group (N=805).

Participants were recruited from 35 general practices located in and around Utrecht, the fourth city in the Netherlands, with over 300.000 citizens. The electronic medical record (EMR data) from the general practitioner (GP) was screened for eligible participants, who had to be aged 60 years and over, and at least one of the following criteria: (1) a frailty index score using the accumulated deficit approach18 with a cut-off of >0.20 19; (2) polypharmacy, defined as five or more different medications in chronic use ; (3) a consultation gap, defined as not having consulted the GP in the past three years, except for the yearly influenza vaccination. The frailty index was constructed according to the Rockwood-approach18 and consisted of a list of 50 items of International Classification of Primary Care (ICPC) and anatomic therapeutic chemical (ATC) codes (18, 19). Exclusion criteria were living in a nursing home or assisted living facility, and terminal illness. Eligible older adults were invited and participated after written informed consent. Data were collected using questionnaires at baseline, six and twelve months after inclusion.

What is aging?

There are a number of parallels between aging in life sciences and in aircraft structures (Table 1). Comparisons between human aging and airplane aging have been established:

Table 1
Aging parallelism

Human Aging	Aircraft Aging
Genes	Design
Growth	Manufacturing
Physician visit	Evaluation (Check)
Preventive Medicine	Maintenance
Hip/Heart	Part replacement
Oxidative damage	Corrosion
Cancer	Radiation damage
Frailty	Fatigue

Aging, in life science, is defined as a progressive decline in physiological function, leading to an age-dependent decrease in rates of survival and reproduction (1). Aging is a process that is genetically determined and environmentally modulated (2).

For human aging, frailty is a clinical state in which there is vulnerability for developing increased dependency and/or mortality when exposed to a stressor (3). Frailty can occur as the result of a range of diseases, medical and environmental conditions. Frailty is a pre-disability status still accessible to preventive measures. It needs to be distinguished from disability which is usually an irreversible condition. The disability process can be slowed by physical and mental exercise but can be accelerated by diseases (4).

To extend lifespan without disability of one individual, overcoming some of the consequences of the aging processes, preventing diseases and associated functional limitations is relevant. This approach has been demonstrated to be especially relevant in the frail elderly population. Different tools have been developed to screen frailty in community-dwelling older population: The Fried's phenotype of frailty (5), The Frailty Index (6) or the IANA – FRAIL scale (7).

In aircraft structures

Aging is defined as a slow alteration of a material chemical or physical structure by the simple effect of time or by special treatment to which it is exposed. These constraints have a detrimental effect on the material properties. It leads to gradual loss of the design function and ultimate failure or unacceptable loss of efficiency (8). Aging may be broadly categorized by three primary mechanisms: chemical, physical and mechanical. The interaction between these three areas is highly dependent on two variables: material characteristics and aging environment (9). The long-term properties of composite materials, when exposed to a combination of in-service loads and environments are still not well characterized. The importance to predict and overcome aging is relevant. Similarly to human aging, different methods have been implemented to detect these early problems: NDT (Non destructive testing methods), e.g., visual, magnetic, radiographic and ultrasonic techniques (10).

How do we predict and study aging?

In life science

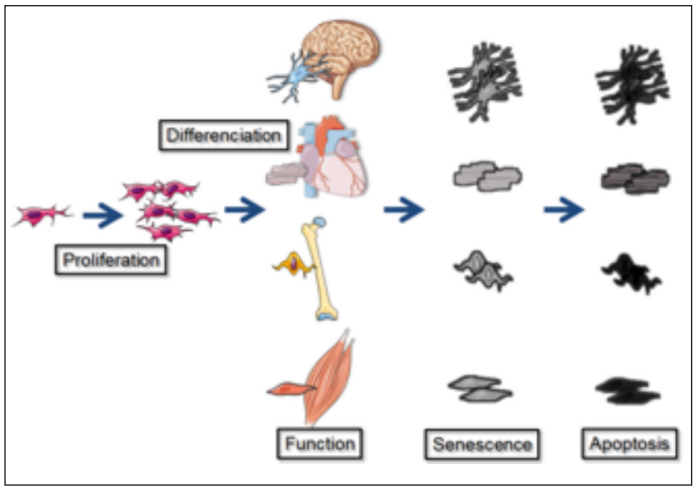
Models and prediction – Animal models of aging

In medicine, Aging is the largest risk factor for numerous human diseases, and understanding the aging process may thereby facilitate the development of new treatments for age-associated diseases. Aging research on humans is complicated by many factors like environmental variability, genetic variability, budget, and ethical factors but moreover, due to their long natural life span. An alternative is to develop and study animal and cellular models of human disease. The cellular models provide relevant information of the mechanisms; however, they do not necessarily replicate the in vivo biology. It is why, as all organisms age, animal models can be useful for studying aging. Exciting research is taking place in variety of species, commonly from yeast to mouse but also in other species closely related to human beings like monkeys.

Several cellular processes are associated to ageing. Among them, cellular senescence imposes permanent proliferative arrest on cells in response to various stressors. Cell senescence has emerged as a potentially important contributor to aging and age-related disease (11).

Cells can be considered as a clock and each cell cycle promotes damage within the cell such as DNA damage, telomere dysfunction, epigenetic changes, deregulation, metabolic defects, stem cell exhaustion, inflammatory effects, and senescence. These damaging effects bring about cell aging and human aging.

Figure 1
What is cell senescence?



One of the approaches to study human aging is to search for organisms as a model. The chosen organisms can be small, inexpensive and experimentally tractable, allowing the manipulation of the factors affecting aging. As they have a short lifespan, scientists can control the environment and minimize the genetic variation by using inbred animals.

Different species are used in animal models. These species have different lifespans due to potential disparities in several physiological mechanisms including:

- Longevity / size relationship
- Longevity / temperature relationship
- Longevity / metabolism relationship.

The points that have been highlighted are:

- The importance of animal model studies for human aging understanding. Simplified models are less complex (phenotype), have shorter lifespan and are affordable (costs).
- In animal models, every environmental parameter is challenged in order to better characterize lifespan differences and assess aging.
- Animal models of aging are precisely studied, from cellular level to intact animal.
- The results can be scaled to human based on mathematical and statistical analysis.

The models that are most used in aging research are yeast, worm (C. elegans), fly (Drosophila melanogaster) and mouse. It has been noted that human and yeast shared pathways of aging (12), that C. elegans lifespan genes have human homologues (13); and the Drosophila insulin-like pathway studies have been highly interesting (14).

In aircraft structures

Qualification rules

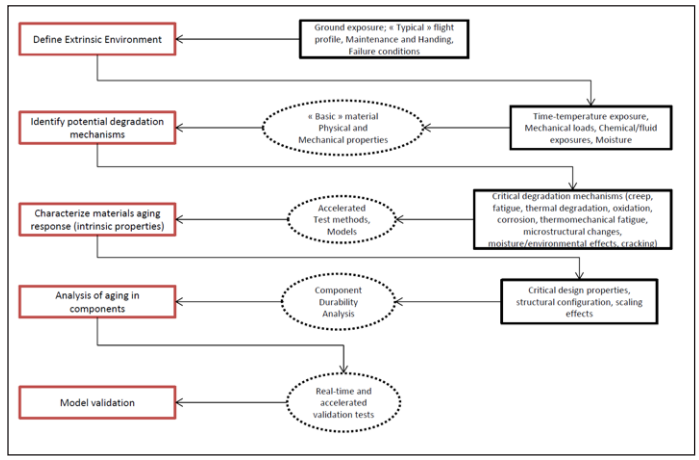
Engineering structures must be capable of performing their function throughout a specified lifetime while meeting safety and economic objectives. These structures are exposed to a series of events that include loading, environment, and damage threats. These events, either individually or cumulatively, can cause structural degradation, and can affect the ability of the structure to perform its function. Since the beginning of aviation, we have been looking for the material the most efficient, the most sustainable, and the less sensitive to environment. Composite is at present the best material and has been developed and used today on aircraft.

The use of commercial aircraft beyond their original design service objective is a new objective for the airlines. For this reason, it is necessary to understand composite aging. The aging will be mainly caused by damages (oxydation), loading (fatigue) and environment conditions (temperature, humidity, radiation….). These events will modify the structure.

The aging of material can be defined as the transformation or the modification of some properties of the material by the simple effect of time or by the special treatment to which it is subjected. The main objective is to ensure the continued operational safety of composite structures as they age. Structures are certified by authorities (FAA for USA and EASA for European Union) in order to ensure safety. There is a constant evolution of regulations. These rules are done by a close cooperation between the authorities and the aircraft manufacturers. Composite structures long-term aging is more and more taken into consideration for certification.

Figure 2

Recommended general approach to characterization on aging of materials and structures (15)



Medialization and prediction

A composite material is constituted of a matrix (organic) and continuous, long or short fibers (glass, carbon). The matrix holds in position the fibers and ensures the load transfer to the fibers. The fibers provide stiffness, strength and anisotropy to the structure. The failure mechanism starts with the matrix cracks, then a delamination stage and finally fiber failure. The Tg (glass transition temperature) is an important parameter of the material and reflects the resin property. The glass transition is linked to the amorphous phase and has a key role on polymer properties. If the temperature is below Tg, the material is in an amorphous state, the material is stiff and brittle. When the temperature is over Tg, we are in the rubbery state. And the material is visco-elastic (flexible and ductile).

There are different types of composite aging. The first is the physical aging which is linked to this glass transition (16) showed that the density of the material increase with ageing time at T>Tg. The material properties thus depend on ageing time. Indeed, the density, stiffness and brittleness increases. The yield stress decrease the toughness decreases severely. This physical ageing is reversible with temperature rejuvenation.

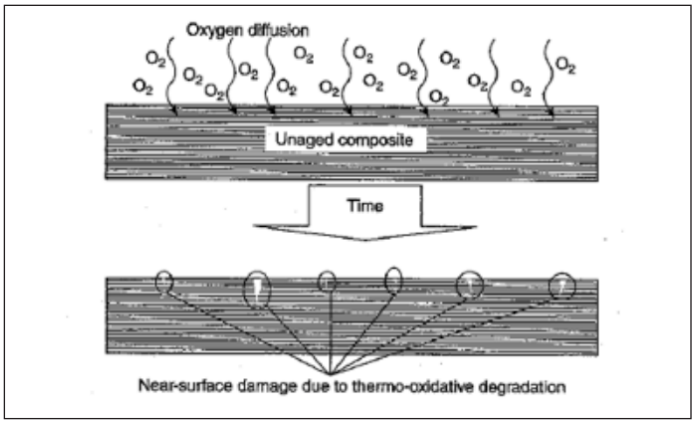
The second aging category is moisture aging which is related to the water absorption in the material modeled by Fick's law. The characteristics of the diffusion in composite is linked to the anisotropy, depends on matrix percentage (~40%). The diffusion is thermal activated and generates a saturation mass

(%VH). The characteristic time diffusion is: 8 days – 1mm, +2 years / 10mm [16]. This moisture degradation is reversible (classically for epoxy resin) and sometimes irreversible (for step-growth polymer and for some thermoplastic). The most relevant effect of moisture aging is the plasticizing effect with a break up of hydrogen bond in the network. The material goes from stiff to flexible, the Tg decreases as well as the matrix young modulus and failure stress.

The next ageing category is Ultraviolet ageing. Composite material is sensitive to photo-oxidation, surface degradation under oxygen or ozone, accelerated with UV exposition. The mechanism is chemical. And the consequences are: a reduction of the polymer's molecular mass, the material is more brittle, leading to a reduction of tensile and impact strength as well as a discoloration and loss of surface smoothness. The effects are limited to surface, and are mainly a concern for painting, for aerodynamics and composite material during production (before painting).

The last ageing category is thermal ageing. For epoxy resin, the degradation mechanisms are post-curing and chain scission. It occurs when the temperature is over 150°C with dioxygen presence. The predominant mechanism is thermo-oxidation. At higher temperatures, there is thermolysis and thermo-oxidation. The thermo-oxidation is controlled by O2 diffusion and interacts with damage that leads to surface cracks.

Figure 3
Thermo-oxidation



The thermal aging effects are (9): a mass loss, Tg evolution, surface appearance and for the mechanical properties we have the diminution of elastic properties, yield strength and toughness.

Below is presented a summary table of the different aging categories.

Table 2
Aging type

Aging type	Where	Effects	T°+Factor
« Physical »	Bulk	Reversible	Endogene
Moisture	Bulk	≈ Reversible	H20
UV Rays	Surface	Irreversible	UV + O2 ,O3
Thermal with O2	Bulk Surface	Irreversible Irreversible	Endogene O2

Aging affects the resin matrix and the fiber/matrix interface and lead to:

- A decrease of properties such as stiffness, strength and toughness.
- A surface alteration and cracks

It is important to note the interaction of environmental effects with mechanical loads, the cyclic environmental conditions. The process of ageing is a time constant process and thus the need of accelerated ageing tests is essential for structures development and certification.

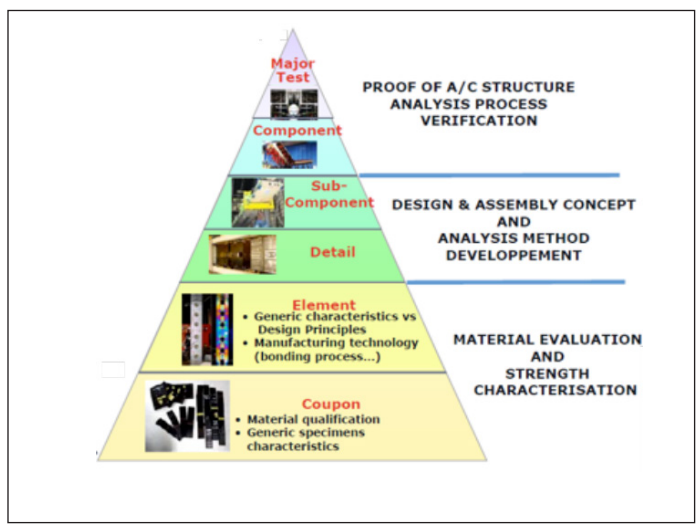
Design solutions

The aircraft structures are exposed to many different stressors (individually or in combination) such as: erosion, aggressive fluids, UV, fire, lightning strike (direct and indirect effect), mechanical loading (including cycling and creep), mechanical impact (in production and/or in-service), temperature and humidity (17, 18).

All these parameters must be addressed in the design of the aircraft.

An extensive test survey is undertaken during the development stage for certification of the aircraft program. The tests performed on the components follow a pyramidal approach. Aged specimens are tested as well.

Figure 4
Pyramidal test approach for airframe qualification



This approach is similar to the development of animal model to study human aging: influential parameters are identified on airframe aging with the building block approach from elementary coupons to large scale tests to support analogies regarding in-service life.

Airbus has developed a number of prevention solutions or demonstrations summarized below:

- Erosion → Anti erosion coating
- Aggressive fluids → No effect worse than moisture
- UV → Anti-UV coating
- Fire → Application of resin as per FST (Fire, Smoke and Toxicity) requirement
- Lightning strike → Protection per layer of metallic foil and design principles
- Mechanical loading → Fatigue testing and design principles
- Mechanical impact → Testing
- Temperature → Mechanical testing on aged specimen and design principles
- Humidity → Mechanical testing on aged specimen and design principles

All these measures constitute a robust approach demonstrated with no in-service issue on more than 230 million flight hours (~26000 years)

In addition to these prevention solutions, the establishment of criteria and models allowing predicting the long-term behavior of composite structures is an important challenge for aircraft manufacturers and authorities. The optimization of the performance of structure components and thus of the materials, on longer operating lives, need robust prediction models, that consider the total of the applied stresses and external environmental threats.

Perspectives, what can we do in practice

Real Time Bone and Composite Repair

One example where the development of in-flight composite repair, which will be essential for long space flights, is the continuous repair process of human bone. The osteocytes are small cells that act as mechanostressors and can recognize cracks in bone. When this happens they activate osteoclasts to clear the damaged bone and osteoblasts to then repair the area (rebuild bone). Composite repair manufacturers are already experimenting with automatic repair for cracks in the fuselage, e.g., Racks of separated epoxy resin and amidomine or microcapsules that release dicyclopentadiene to interact with a ruthenium catalyst. Nanobots modeled on bone cell remodeling may prove to be an even more effective method for in-flight repair.

Determinants

Many factors combine together to affect the health of individuals and communities. Whether people are healthy or not, health status is determined by circumstances and environment. To a large extent, factors such as where we live, the state of our environment, genetics, our income and education level, and our relationships with friends and family all have considerable impacts on health, whereas the more commonly considered factors such as access and use of health care services often have less impact (19, 20).

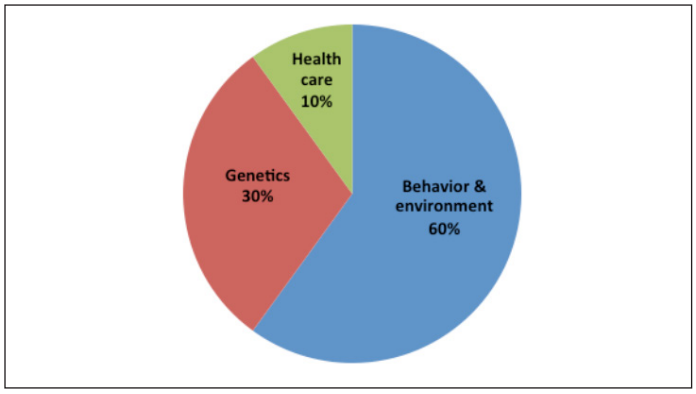
The determinants of health include:

- The social and economic environment,
- The physical environment, and
- The person's individual characteristics and behaviors.

Extensive studies have been conducted showing that health prospects have been shaped by five domains: genetic and gestational endowments, social circumstances, environmental conditions, behavioral choices, and medical care (21, 22). These determinants of health have been identified and quantified (23, 24). It is now quite clear that when the objective is to reduce early deaths, medical care has a relatively minor impact. The greatest opportunity to improve health and reduce premature deaths depends on personal behavior. Behavioral causes account for nearly 40% (obesity, tobacco…) of all deaths in the United States (24).

Figure 5

Health determinants in U.S (25)



The identification of health determinants is precious information for aging assessment. Whether the parallelism can be made about aircraft aging remain an open question. However, establishing the weight of each determinant on "Health" or "Quality" of airframe and by extension the whole aircraft would be helpful to give direction to research programs.

P4 Systems approach

Medicine is an old discipline but also a fast-evolving sector. Medicine is increasingly moving from a reactive to a proactive approach discipline over the next decade, becoming a predictive, personalized, preventive and participatory, the so-called P4 medicine (Table 3) (26).

Figure 6
Aircraft "health" determinants

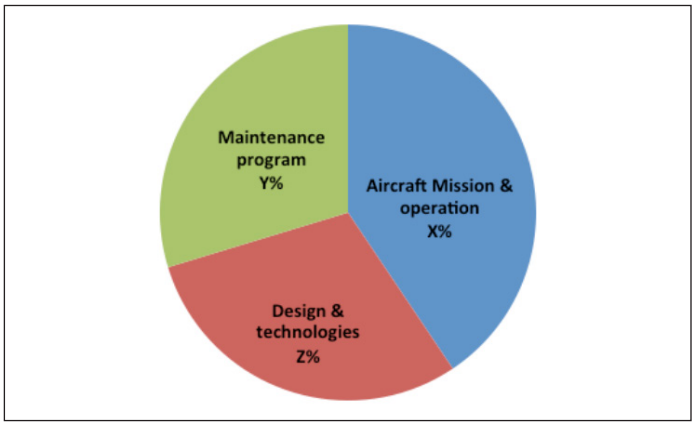


Table 3
P4 medicine vs Today medicine

P4 medicine	Today medicine
Proactive, predictive (very early stage)	Reactive
Individual, precision medicine	Population
Wellness & diseases	Only diseases
Personalized data clouds	Average patient population
Personalized data clouds for clinical trials	Averaged patient population for clinical trials

P4 medicine is based on systems approaches to disease, emerging technologies and analytical tools.

Systems medicine abilities are to:

- Provide deep insight in the disease mechanisms
- Make blood a diagnostic window for viewing health and disease for the individual
- Stratify complex diseases into their distinct subtypes for a impedance match against proper drugs
- Provide new approaches to drug target discovery
- Generate metrics for assessing wellness.

Two of the clinical objectives of P4 medicine are to quantify wellness and to demystify disease (27).The two main challenges utilizing P4 medicine are technical (digital revolution, big data) and societal barriers (sharing data). Societal barriers will be the most challenging. In order to bring different parts (patients, physicians, health-care members) to align with P4 medicine, new strategic partnerships have to be created (large clinical centers and patient-advocate groups).

As for aeronautics, the system approach is a key for a better maintainability. It is important to avoid separated non-crossing tasks like illustrating below that unable actor to see the global issue.

Aeronautics use since long time system approaches. However, can we develop even more the aircraft system approach with the P4 points? This approach needs a different mindset as earlier check should be done, and aircraft operation can be potentially modified. Success of this approach is based on partnership. P4 medicine is patient participatory-based. This means that support should be given to airlines to improve aircraft life.

Table 4
P4 maintenance vs Today maintenance

P4 Maintenance	Today Maintenance
Proactive, predictive (very early stage)	Reactive
Singular A/C	A/C Fleet
Performance & damages	Only defects, damages
Singularized data clouds	Average fleet surveys
Singularized data clouds for performance surveys	Averaged fleet population for surveys

Conflict of Interest: ???????

Ethical standard: ??????.

References

1. Rose M. R. Evolutionary Biology of Aging. New York: Oxford University Press. 1991
2. T. Kirkwood. Understanding the Odd science of Aging. Cell, Vol.120, No. 4, 2015;pp 437-447.
3. Rosado-Artalejo, C., Carnicero, J.A., Losa-Reyna. Global performance of executive function is predictor of risk of frailty and disability in older adults. J Nutr Health Aging, 2017.
4. J. Morley et al. Frailty consensus: a call to action, Journal of the American Medical Directors Association, 2013;Vol.10, p142.
5. LP. Fried. Frailty in older adults: evidence for a phenotype, The journals of gerontology. Series A, Biological sciences and medical sciences, 2001;Vol.56, No.3, pp146-156.
6. K. Rockwood, A. Mitniski et al. Some mathematical models of frailty and their clinical implications. Reviews in Clinical Gerontologyl, 2002;vol.12, pp109-117.
7. G. Abellan van Kan, Rolland Y et al. The I.A.N.A Task Force on frailty assessment of older people in clinical practice, Journal of Nutrition Health and Aging, 2008;Vol. 12, No.1, pp 29-37.
8. E. David. Aging of polymeric materials: principles. Université du Quebec. 2009
9. T. Gates, The physical and chemical ageing of polymeric composites, NASA Langley Research Center, Ageing of composites, Whoodhead publishing, 2008.
10. C. Garnier, ML. Pastor et al. The detection of aeronautical defects in situ on composite structures using Non Destructive Testing, Composite structures, 2011;Vol.93, No.5, pp1328-1336.
11. B. Childs, M. Durik et al. Cellular senescence in aging and age-related disease: from mechanisms to therapy, Nature Medecine, 2015;Vol.21, No. 12, pp1424-1435.
12. J. Myeong. High-throughput analysis of yeast replicative aging using a microfluidic system, Proceedingd of the National Academy of Sciences of the United States of America, 2015;Vol.112, No.30, pp8364-9369.
13. C. Kenyon, J. Chang et al. A C. elegans mutant that lives twice as long as wild type. Nature, 1993;Vol. 366, No. 6454, pp461-464.
14. M. Tatar. A mutant Drosophila insulin receptor homolog that extends life-span and impairs neuroendocrine function, Science, 2001;Vol.292, No.5514, pp107-110.
15. National Material Advisory Board. Accelerated aging f materials and structures, NRC, 1996.
16. G. Odegard, A. Bandyopadhay. Physical aging of epoxy polylmers and their composites, Journal of polymer science Part B: Polymer physics, 2011;Vol. 49, No. 24, pp1695-1716.
17. J. Pascault. Influence of hydrothermal ageing and thermal treatments on the viscoelastic behavior of DGEBA-MCDEA epoxy resin. Polymer Bulletin.

2002;Vol.48, No.1, pp75-82.
18. T. Tsotsis. Thermo-oxidative ageing of composite materials. The Boeing Company. Ageing of composites, Whoodhead publishing, 2008.
19. World Health Organization, Health Impact Assessment.
20. Hajek, A., Luck, T., Brettschneider, C. et al. J Nutr Health Aging, 2017;21: 299.
21. J.M. McGinnis, "United States," in Critical Issues in Global Health, ed. C.E. Koop (San Francisco: Jossey-Bass, 2001;pp 80–90
22. Kucukerdonmez, O., Navruz Varli, S. & Koksal, E. Comparison of nutritional status in the elderly according to living situations. J Nutr Health Aging 2017;21: 25
23. J.M. McGinnis, P. Williams-Russo, J.R. Knickman. The case for more active policy attention to health promotion, Health Affairs, 2002;Vol. 21, No. 2, pp78-93.
24. S. Schroeder, We can do better – Improving the health of the American people, The New England Journal of Medicine, 2007;Vol. 357, No. 12, pp1221-1228.
25. L. Hood. Systems medicine and pro-active P4 medicine: transforming healthcare with scientific wellness – a personal journey. 13th Nestle International Nutrition Symposium, 2016.
26. L. Hood, S.H. Friend. Predictive, personalized, preventive, participatory (P4) cancer medicine. Nature Reviews. Clinical Oncology. 2011;Vol. 8, pp 184–187.
27. L. Hood, M. Flores. A personal view on systems medicine and the emergence of proactive P4 medicine: predictive, preventive, personalized and participatory. New Biotechnology, 2012;Vol. 00, No. 00.