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Contents

Vsebina

Izvirni znanstveni članek ■

Populacije orjaških lipidnih veziklov kot model za študij bio-nano interakcij

Jernej Zupanc, Damjana Drobne

Izvleček. Vse več študij prihaja do ugotovitev, da interakcije z nanodelci vplivajo na stabilnost celičnih membran. Namesto izpostavljanja živih organizmov se za preučevanje interakcij z nanodelci pogosto uporabljajo lipidni vezikli kot model celičnih membran. Predstavljena računalniško podprta metodologija omogoča zaznavanje in kvantificiranje morfoloških sprememb tisočev veziklov skozi čas izpostavljenosti nanodelcem. Zajema korake od eksperimentalnega protokola preko računalniške obdelave mikrografij do analize pridobljenih podatkov. Namen dela je bil ugotoviti morebiten vpliv dveh tipov nanodelcev (C_{60} in $CoFe_2O_4$) na POPC lipidne vezikle s študijo populacije veziklov namesto izoliranih posameznikov. V predstavljenih eksperimentih ugotavljamo, da oba preizkušena tipa nanodelcev vplivata na morfološke spremembe ali pokanje lipidnih veziklov.

Giant Lipid Vesicle Populations as a Model for Bio-nano Interaction Studies

Abstract. Recent evidence suggests that nanoparticles affect cell membrane stability and subsequently exert toxic effects. To assess these interactions, research is often conducted on lipid vesicles as substitutes for cells. We present a methodology that enables observing thousands of lipid vesicles and analysing their shape transformations with the use of computerised image processing and data analysis. Our aim was to test whether this approach is appropriate for assessing effects of nanoparticles (C_{60} and $CoFe_2O_4$) on POPC lipid vesicles. In the presented experiments, we show that nanoparticles provoked bursting of vesicles as well as changes in their size and morphology. The novelty of our approach lies in the possibility to investigate a large population of vesicles and generate statistically relevant results. Our data demonstrates that nanoparticles affected lipid membranes and may have a potential to affect cell membranes as well.

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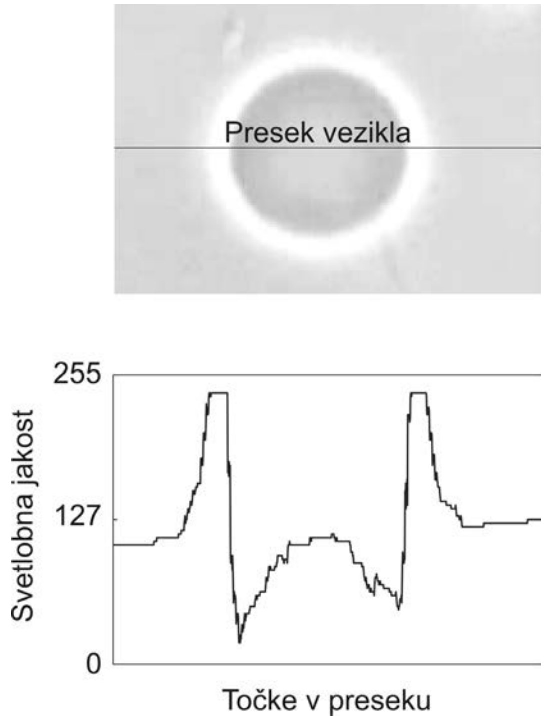
Uvod

Nanotehnologija je panoga, ki razvija, opredeljuje in proizvaja materirale v velikostih 1-100 nanometrov. Materiali v tem velikostnem razredu spremenijo lastnosti v primerjavi z večjimi materiali iste kemijske sestave, kar jih naredi zanimive za širok spekter uporabe v zdravstvu, kozmetični industriji, proizvodih vsakdanje rabe, elektrotehniki, proizvodnji energije idr. Lastnosti nanodelcev hkrati z njihovo veliko reaktivnostjo istočasno predstavljajo možnosti za nove tipe interakcij z biološkimi sistemi. Te interakcije so povsem neznane in zato v zadnjem času v ospredju številnih raziskav.[1] Nedavno je bilo ugotovljeno, da pri interakcijah z živimi bitji nanodelci najprej stopijo v stik s celičnimi membranami in posledično povzročijo verigo celičnih sprememb.[2] Za natančno preučevanje interakcij med celičnimi membranami in različnimi substancami so uveljavljen model umetni lipidni vezikli.

Lipidni vezikli

Lipidni vezikli so mehurčki, narejeni iz enakih lipidov, kot jih najdemo v celičnih membranah (slika 1). V raziskavah in aplikacijah so pogosto uporabljeni kot poenostavljeni modeli celic.[3,4] Na širokem področju raziskav celičnih membran, izpostavljenih različnim pogojem, postajajo zelo priljubljen nadomestek celic. Zaradi ustrezne velikosti jih lahko neposredno opazujemo pod svetlobnim mikroskopom. Običajno raziskovalci osamijo vezikel ali manjšo skupino, jo izpostavijo spremembi okolice ter skozi daljše časovno obdobje spremljajo spremembe, saj je pričakovati specifičen časovno pogojen vpliv.[5,6]



Slika 1 Zgoraj: orjaški lipidni vezikel premera 10 μm, posnet s faznokontrastnim mikroskopom. Vodoravna črta označuje presek in poteka skozi ozadje mikrografije, obroč vezikla in notranjost vezikla. Spodaj: svetlobna jakost točk v zgoraj označenem preseku. Na vodoravni osi so vrednosti od 0 (črnina) do 255 (belina). Različne svetlobne jakosti delov mikrografije lahko uporabimo za segmentacijo posameznih objektov, v tem primeru vezikla.

Pri proučevanju vpliva nanodelcev je smotrno opazovati večjo skupino veziklov, saj tip interakcij ni poznan niti ni nujno, da je učinek enak pri vseh veziklih. Zaradi specifičnosti nanodelcev in njihovih še neznanih interakcij z lipidnimi membranami[7] je za proučevanje interakcij zelo primereno opazovanje skupine veziklov namesto osamljenih primerkov. Namen našega dela je bil ugotoviti morebiten vpliv dveh tipov nanodelcev na umetne lipidne vezikle in pokazati uporabnost preučevanja oblik in velikosti veziklov v populacijah tisočih veziklov za študij vpliva nanodelcev na lipidne membrane. Naš pristop je temeljil na zajemanju slike populacije veziklov v določenih časovnih obdobjih. Na podlagi posnetka ob vsakem obdobju smo naredili statistično analizo morfoloških značilnosti veziklov[8,9,10,11] in preučevali občutljivost in primernost računalniškega pristopa k zajemu in obdelavi slik veziklov za namene ugotavljanja vplivov nanodelcev na biološke membrane.

Tu predstavljamo računalniško podprto metodologijo za proučevanje populacij lipidnih veziklov in navajamo rezultate, ki smo jih pridobili z njeno uporabo pri ugotavljanju posledic interakcij lipidnih veziklov z različnimi nanodelci. Predstavljena metodologija vključuje protokol za izvedbo poskusa in zajem mikrografij ali mikrografskih videoposnetkov ter računalniške pristope za analizo populacij veziklov iz pridobljenih posnetkov (slika 2).

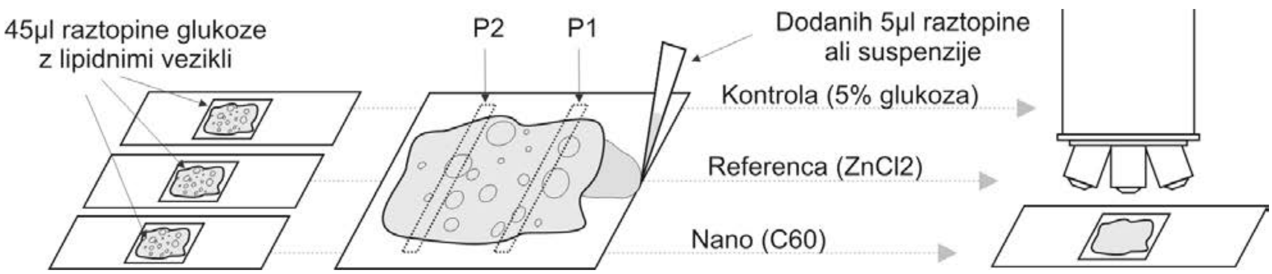
Slika 2 Potek korakov v predstavljeni metodologiji za analizo populacij lipidnih veziklov. Potemnjeni pravokotniki predstavljajo korake, poševni tisk pa njihove izhode.

Eksperimentalni protokol

Prvi korak metodologije je izvedba eksperimenta, v katerem izpostavimo populacije lipidnih veziklov nanodelcem ter naredimo mikrografske posnetke, ki služijo za nadaljno računalniško obdelavo. Izvedli smo dva poskusa s populacijami lipidnih veziklov in različnimi nanodelci. V enem smo raziskovali interakcije veziklov s C_{60} nanodelci (fulereni), v drugem pa s kobalt-feritnimi ($CoFe_2O_4$) nanodelci. Razlike med poskusoma so navedene v tabeli 1, v nadaljevanju pa je predstavljen protokol, ki je enak za oba poskusa.

Orjaški unilamelarni fosfolipidni vezikli so pripravljeni iz 1-palmitoil-2-oleoil-sn-glicero-3-fosfatidilholina (POPC) in holesterola, zmešanih v razmerju 4:1 na sobni temperaturi s prilagojeno metodo elektroformacije.[12,13] Po preteku 24 ur od začetka priprave veziklov izvajamo eksperiment. Za vsako populacijo (npr. kontrolno, referenčno, nano) pripravimo po eno objektno stekelce, na katerega namestimo 45 μl veliko kapljico suspenzije z vezikli. Na vzorec poveznemo manjše objektno stekelce, ob straneh pa prostor z vzorcem zapremo s silikonsko pasto, da preprečimo izhlapevanje.

Na shemi (slika 3) je prikazan potek poskusa s C_{60}, kjer enakim populacijam veziklov dodamo različne aditive. Na vsakem stekelcu določimo sled (P1) v bližini dodanega aditiva, kjer poteka snemanje. Če je sledi več (P1, P2, ...), so izbrane nekaj milimetrov narazen, kar omogoči spremljanje vpliva koncentracijskega gradiena aditiva na vezikle. Nato pod 400-kratno povečavo fazno kontrastnega svetlobnega mikroskopa posnamemo enodimenzionalno sled, v kateri je zajet vzorec populacije veziklov.



Slika 3 Vrstni red korakov v primeru eksperimenta s populacijami lipidnih veziklov in C_{60} nanodelci. Najprej razdelimo enako količino suspenzije glukozne raztopine in lipidnih veziklov na tri stekelca. V naslednjem koraku dodamo vsakemu vzorcu nanodelce ali referenčno kemikalijo (služi kot pozitivna referenca) in glukozno raztopino (služi kot kontrola). Določimo sledi na vzorcu, kjer zajemamo slike ali videoposnetke populacije. Pri eksperimentu s $CoFe_2O_4$ ni bilo populacije z referenčno kemikalijo. Prav tako smo zajeli le P1. Shema ni v merilu.

Snemanje ponovimo večkrat – po preteku določenih časovnih obdobij (za oba poskusa so navedena v tabeli 1), da zajamemo spremembe v populacijah skozi čas. Prvo obdobje zajema je po dodajanju veziklov na objektno steklo, drugo po dodajanju nanodelcev. Poleg tega snemamo populacije veziklov tudi po večdesetminutni izpostavitvi dodanim substancam. Posnete mikrografije ali videi so osnova, ki jo pozneje računalniško obdelamo, da izločimo podatke o zajetih populacijah veziklov.

Tabela 1 Razlike in podobnosti dveh poskusov z nanodelci in populacijami lipidnih veziklov.

Poskus	Zajem posnetkov	Čas ob zajemanju (min)	Referenčna kemikalija
C_{60}	810 mikrografij	1; 10; 100	$ZnCl_2$
$CoFe_2O_4$	6 videoposnetkov	1; 90	brez

Pri eksperimentih z nanodelci smo uporabili različna načina snemanja populacij. V eksperimentu s C_{60} smo na vsaki sledi zajeli po 15 mikrografij, v eksperimentu s $CoFe_2O_4$ pa petminutni videoposnetek. Z zajemom posameznih mikrografij smo zajeli približno 15 % sledi, videoposnetek pa zajema celotno sled. V primeru posameznih mikrografij je za analizo populacije potrebna le še segmentacija veziklov, videoposnetek pa moramo najprej zlepiti v veliko sliko (mozaik), iz katere nato segmentiramo vezikle. V naslednjem razdelku je opisan postopek lepljenja videoposnetka v mozaik, ki se nanaša na eksperiment s $CoFe_2O_4$. Pri eksperimentu s C_{60} ta korak ni bil potreben, saj se iz posameznih mikrografij (za razliko od videoposnetka) lahko takoj segmentira vezikle.

Računalniško procesiranje

Proučevanje vzorca, ki je večji od vidnega polja na izbrani povečavi pod mikroskopom, kamor spadajo tudi populacije lipidnih veziklov, je izvedljivo z lepljenjem posameznih mikrografij v veliko sliko – mozaik. Pristop je bil uporabljan med fotografi že v 19. stoletju, v 20. stoletju pa so ga prevzeli tudi znanstveniki in dandanes je v uporabi na mnogih znanstvenih področjih. V mikroskopiji lahko mozaik večjega opazovanega vzorca naredimo tako, da vzorec premikamo pod mikroskopom in zajemamo delno prekrivajoče mikrografije. Slednje kasneje zlepimo v mozaik z uporabo komercialnega programskega orodja[14] ali pa razvijemo algoritem, posebej namenjen lepljenju mikrografij, specifičnih za naš vzorec.[15-19] Poleg slik lahko za lepljenje mozaikov uporabimo tudi mikroskopske videoposnetke,[20,21] kjer je pristop podoben, a zahtevnejši kot lepljenje iz posameznih slik.

Dinamična narava veziklov zahteva zajem čim večjega vzorca v čim krajšem času, kar lažje dosežemo z videoposnetki kot s posameznimi mikrografijami. Ker segmentacijo veziklov izvajamo iz slik, je potrebno videoposnetek zlepiti v veliko sliko – mozaik, ki predstavlja celotno posneto področje.

Pretvorba videoposnetka v mozaik

Pri lepljenju videoposnetka populacije lipidnih veziklov v mozaik, se pojavijo naslednji problemi:

- Odstranjevanje digitalne nečistoče z videoposnetkov. Nečistoča je posledica prašnih delcev v optičnem in snemalnem delu mikroskopa.
- Razrez videoposnetka na manjše dele za pohitritev procesiranja in sestavljanje prvotnega medianskega mozaika,
- detekcija veziklov v mozaiku,
- iskanje najostrejših slik vsakega vezikla v videoposnetku,
- zlivanje najostrejših slik veziklov v končni mozaik.

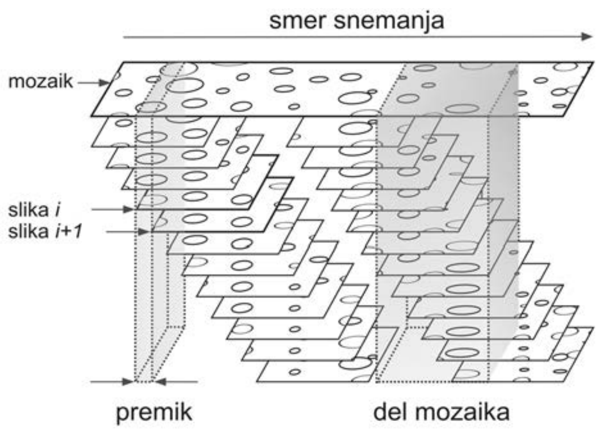
Vhodni podatek v procesiranje je enorazsežni videoposnetek sledi s populacijo lipidnih veziklov. Zaželeni izhodni podatek je velika slika – mozaik, ki predstavlja celotno posneto področje (slika 4). Vsaka slika vezikla v zaželenem mozaiku mora biti njegova najostrejša slika v videoposnetku.

Za odstranitev digitalne nečistoče z videoposnetkov najprej izdelamo sliko nečistoče. Iz naključnega izbora 300 slik videoposnetka izračunamo za vsako točko časovno mediano vseh istoležnih točk. Točke skupaj sestavljajo sliko nečistoče, ki jo odštejemo od vsake slike videoposnetka, da dobimo slike brez nečistoč.

Za lepljenje slik v mozaik potrebujemo podatek o njihovem medsebojnem prekrivanju. Da bi dobili položaj posamezne slike videoposnetka v mozaiku, uporabimo registracijo slik. Med vsakima zaporednima slikama izračunamo normirano križno korelacijo, iz katere lahko razberemo, v kolikšni meri se prekrivata in kakšen je med njima premik (slika 5). Iz vsote zaporednih premikov lahko za vsako sliko videoposnetka določimo njen položaj v mozaiku.

Slika 4 Izsek mozaika zlepljenega iz mikroskopskega videoposnetka sledi ene populacije veziklov. Celoten mozaik je približno 33-krat višji. Obrobljeni pravokotnik na sredini prikazuje velikost polja, kot ga lahko na 400-kratni povečavi vidimo pod mikroskopom.

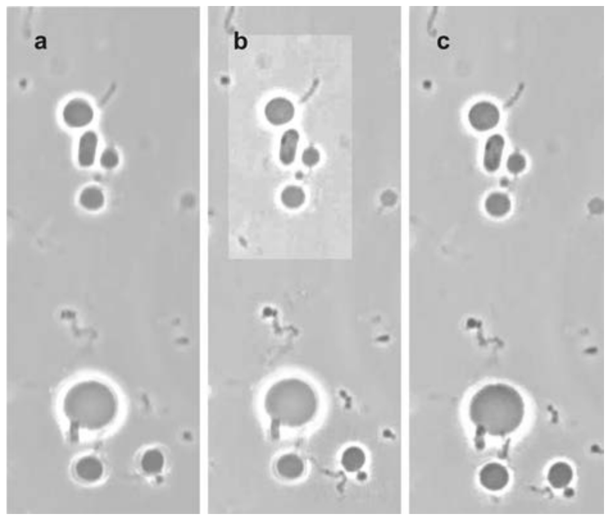
Povprečen videoposnetek posamezne sledi je dolg 5 minut, kar ob 25 slikah na sekundo pomeni 7500 slik. Dimenzije mozaika tako presegajo 40.000 × 2.000 točk, zaradi česar je procesiranje mozaika časovno zelo zahtevno. Postopek pospešimo tako, da vse korake lepljenja mozaikov (in pozneje tudi detekcijo veziklov) izvajamo le na posameznih delih mozaika naenkrat (slika 5). Za določitev teh delov je potrebno poiskati področja posnetka brez veziklov, kjer bodo potekale meje med deli. Zaradi enorazsežne narave videoposnetka mozaik razrežemo na dele po krajši dimenziji (posnetek, ki poteka navpično kot na sliki 4, režemo vodoravno). Za vrstice razreza izberemo tiste z najmanjšo varianco v svetlobni jakosti. Vrstice, kjer je svetlobna jakost najbolj homogena, so namreč vrstice, kjer vezikli ne nastopajo (ozadje posnetka je homogeno, svetlobna jakost v območju veziklov pa se spreminja – slika 1). Z razrezi v teh vrsticah zagotovimo, da noben vezikel ni v posameznem delu le polovično, kar bi izničilo verodostojnost končnega mozaika.



Slika 5 Interpretacija slik videoposnetka. Zgornja puščica označuje smer snemanja, pod njo pa je prikazan zajeti mozaik. Pod mozaikom so nanizane poravnane posamezne slike videoposnetka in v levem zatemnjenem kvadru je posebej označen premik med dvema zaporednima slikam. V desnem zatemnjenem kvadru je del mozaika, ki vsebuje več slik. Pri lepljenju posameznih slik se na medianski mozaik preslika mediana vseh istoležnih točk prekrivajočih se slik.

Da bi dobili mozaik, je potrebno vse slike videoposnetka združiti v celoto. Vsaka točka mozaika se namreč pojavlja tudi v več sto slikah, v katerih ima pogosto različne vrednosti. Za vsako točko mozaika njeno svetlobno jakost izračunamo kot mediano vseh istoležnih točk v slikah videoposnetka. Tako dobimo prvi, “medianski” mozaik (sliki 5 in 6a), ki pa ni najostrejši. Zaradi uporabe časovne mediane (na sliki 5 si lahko predstavljamo, da poteka navpično) so vezikli v mozaiku neostri, kar onemogoča natančno segmentacijo njihovih oblik.

Naslednji koraki so namenjeni izostritvi veziklov v medianskem mozaiku. Najprej na vsakem delu mozaika naredimo detekcijo objektov (večina objektov so vezikli, nekaj pa je tudi delcev zlepljenih fosfolipidov ali drugih tujkov). Detekcija temelji na izračunu gradientov svetlobne jakosti v vsaki točki, povezovanju točk z najočitnejšimi gradienti v robove (detekcija robov Sobel) in na povezovanju robov, ki so si dovolj blizu, v objekte z uporabo morfoloških operatorjev. Tako zaznamo vse objekte v mozaiku, ki s svojo svetlobno heterogenostjo odstopajo od homogenega ozadja (sliki 1 in 4).



Slika 6 (a) Medianski mozaik; (b) najostrejše slike veziklov, prilepljene na medianski mozaik; (c) najostrejše slike veziklov, zlite v medianski mozaik z gradientnim zlivanjem.

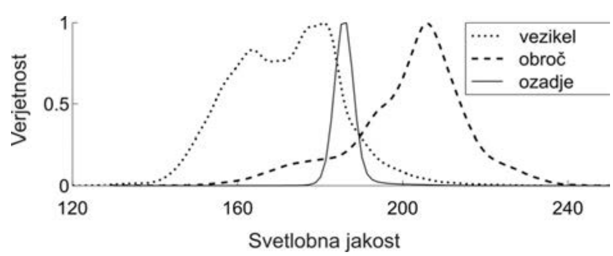
Zaradi inkubacije v tekočini se vezikli v mediju premikajo, kar se pozna tudi na medianskem mozaiku. Tudi ko posamezne slike videoposnetka poravnamo na osnovi izračunanega premika med slikami, ugotovimo, da so posamezni vezikli v slikah neporavnani. Da bi lahko izbrali sliko, na kateri je vezikel najostrejši, je potrebno isti vezikel poravnati v vseh slikah, kjer nastopa. To naredimo z lokalno detekcijo premika. Najprej vsako sliko poravnamo z medianskim mozaikom, tako da so vezikli, ki smo jih našli v prejšnjem koraku, približno istoležni. Za natančno poravnavo izračunamo normalizirano križno korelacijo med območjem okoli vsakega najdenega vezikla in istim območjem v posamezni sliki. Rezultat je lokalni premik vezikla v sliki glede na medianski mozaik. Z uporabo globalnega premika slike in lokalnega premika vezikla lahko slednjega v vsaki sliki natančno poravnamo. Med natančno poravnanimi slikami veziklov je potrebno izbrati najostrejšo. Ta korak je za človeško oko preprost, za avtomatsko računalniško presojo pa je potrebno slike vezikla pretvoriti v število – mero. Izračunane mere slik vezikla nato med sabo primerjamo in izberemo najostrejšo. Preizkusili smo več mer izostrenosti mikroskopskih slik[22] in izbrali mero gradient Brenner, ki se je za določanje ostrine veziklov izkazala kot najprimernejša.

Ko so najostrejše slike posameznih veziklov izbrane, jih je potrebno zliti v medianski mozaik. Če posamezno sliko preprosto prilepimo na mozaik, nastanejo svetlobna neujemanja na robovih lepljenja (slika 6b), zato takšen pristop ni najprimernejši. Takšno neujemanje nastane zaradi različnih nivojev svetlobne jakosti v slikah (medianski mozaik in slika najostrejšega vezikla). V izogib nekonsistencam na robovih se za zlivanje slik pogosto uporablja gradientno ali Poissonovo zlivanje.[23] Namesto da bi iz obeh slik vzeli direktno svetlobno jakost, v eni izmed njih izločimo le svetlobni gradient. V primeru veziklov vzamemo svetlobno jakost mozaika in gradient vezikla. Tako iz svetlobnih jakosti na robovih vezikla v mozaiku z uporabo gradienta iz slike najostrejšega vezikla izračunamo nove vrednosti točk vezikla v mozaiku. Rezultat takšne gradientne interpolacije omogoča najostrejše slike objektov v medianskem mozaiku brez vidnih robov, kjer nastopa zlivanje (slika 6c).

Segmentacija veziklov

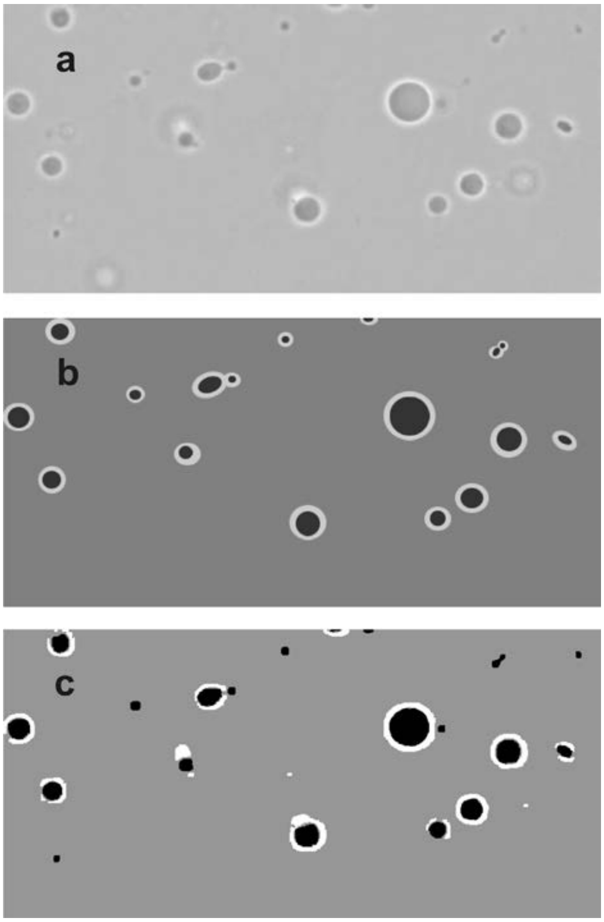
Ko je videoposnetek zlepljen v mozaik z ostrimi slikami veziklov, nastopi problem segmentacije veziklov. Isti korak je potreben tudi za segmentacijo veziklov iz posameznih mikrografij. Problema segmentacije lipidnih veziklov iz mikroskopskih slik so se v literaturi lotili mnogi, največkrat s pomočjo svetlečega obroča, ki nastane okoli veziklov na slikah, posnetih s faznokontrastnim mikroskopom.[5,6,24-26] Svetlobna jakost preseka slike vezikla ima na vsaki strani obliko sigmoide (slika 1), saj je notranjost veziklov temnejša od okolice (kemijska sestava medija v okolici veziklov se razlikuje od tiste v notranjosti vezikla). Omenjeno lastnost avtorji uporabijo tako, da njihov algoritem obriše vezikel iz začetne ročne inicializacije njegovega roba. Peterlin *et al.* [6] so za segmentacijo vezikla iz slik videoposnetka uporabili prilagodljiv prag svetlobne jakosti v sliki skupaj z detektorjem robov Sobel. Takšni pristopi k segmentaciji veziklov so se izkazali za uspešne, vendar je na tem mestu potrebno dodati, da so se avtorji ukvarjali s segmentacijo enega samega vezikla in pogostokrat z ročno inicializacijo njegovega obroča. Kadar segmentacija ni omejena le na izolirane vezikle, pristopi, ki so vezani na njihovo predvidljivo sferično obliko, odpovedo. Prav tako je neuporabna ročna inicializacija tisočih veziklov.

Za našo segmentacijo populacije veziklov smo se zato osredotočili na lastnost veziklov v mikrografijah, ki je skupna vsem, ne glede na njihovo obliko. Porazdelitvi svetlobne jakosti dveh segmentov mikrografij (vezikla in obroča) sta si v vseh primerih zelo podobni. Obroč je svetlejši od ozadja, notranjost vezikla pa temnejša (slika 7). Za segmentacijo populacije veziklov smo izbrali model Markovovega naključnega polja (MRF),[27] ki poleg porazdelitev svetlobnih jakosti posameznih segmentov slike upošteva še sosednost točk v slikah.



Slika 7 Porazdelitvena verjetnostna funkcija svetlobne jakosti za tri segmente mikrografij: vezikle, obroča in ozadja mikrografij.

Sliko (posamezno mikrografijo ali mozaik) želimo razdeliti na tri segmente, katerih verjetnostne porazdelitve svetlobnih jakosti se razlikujejo: vezikel, obroč in ozadje. Ideja modela Markovovega naključnega polja je naslednja. Svetlobna jakost vsake točke slike z določeno verjetnostjo pripada enemu izmed segmentov. Naloga je poiskati največjo skupno verjetnost vseh točk z upoštevanjem znanih verjetnostnih porazdelitev svetlobnih jakosti posameznih segmentov, svetlobnih jakosti posameznih točk in povezav med sosednimi točkami.



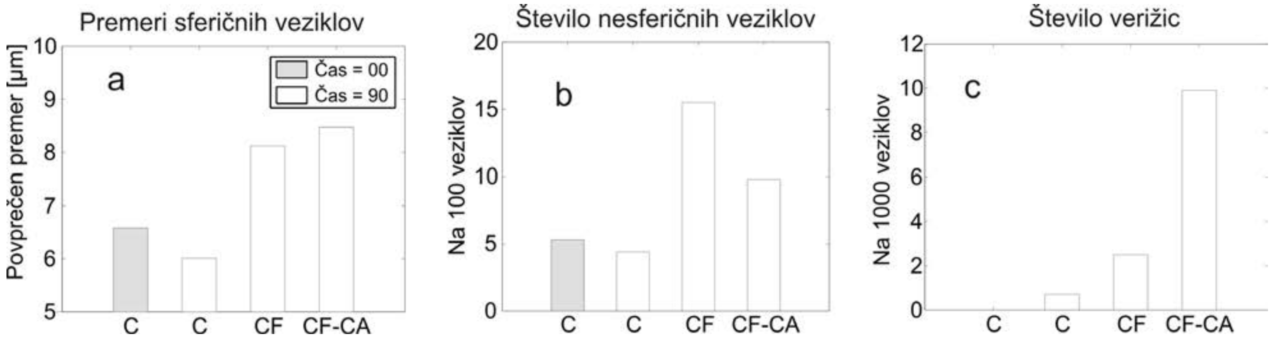
Slika 8 (a) Mikrografija z lipidnimi vezikli; (b) ročno segmentirana mikrografija s tremi segmenti: ozadje, obroč, vezikel; (c) mikrografija, avtomatsko segmentirana z metodo Markovovega naključnega polja.

Iskanje rešitve (segmentacije, ki ima največjo verjetnost glede na navedene pogoje) lahko prevedemo v minimizacijo energije, ki jo sestavljata dva člena. Prvi člen je vsota prispevkov vseh posameznih točk, ki je obratno sorazmerna z razdaljo njihove svetlobne jakosti od povprečja jakosti segmenta, ki mu pripada (slika 7). Drugi člen so prispevki homogenosti segmentov, ki jim pripadajo posamezne točke in njeni neposredni (soseščina osmih točk) sosedi. Energijsko funkcijo sestavimo kot smo opisali drugje,[28] rezultat segmentacije pa je viden na sliki 8. Za pospešitev in izboljšanje natančnosti segmentacije MRF segmentacijo izvedemo le na okolici posameznih veziklov in ne na celotni mikrografiji istočasno. Okolico posameznih veziklov detektiramo z uporabo gradientov, robov in morfoloških operatorjev, kot je opisano v prejšnjem razdelku.

Celoten postopek je načrtovan tako, da segmentiramo vse objekte – tako vezikle, kot vse ostalo, kar izstopa iz ozadja. Tako segmentacija ne obsega le veziklov, ampak tudi nekatere tujke, ki so prisotni v vzorcu. Iz mozaikov ali mikrografij z vezikli izločimo vse segmentirane točke in izračunamo površino, ki jo zasedajo. Tako dobimo število veziklov in njihove velikosti. Po računalniški segmentaciji operater pregleda in popravi segmentacijo – večinoma tako, da izbriše vse označbe, ki niso vezikli. S takšno ročno korekcijo, ki zahteva približno osemkrat manj časa kot celotna ročna segmentacija, zagotovimo njeno natančnost in verodostojnost pridobljenih podatkov.

Rezultati in razprava

Naš MRF algoritem segmentira vezikle vseh oblik – ne ločuje med sferičnimi vezikli, hruškami, verižicami in drugimi. V večini vzorcev je več kot 90 % veziklov sferičnih. Če nas zanimajo tudi vezikli ostalih oblik, jih mora operater po avtomatski segmentaciji označiti s posebno barvo. Tako z minimalnim delom operaterja dobimo tudi kategorizacijo veziklov po oblikah. Iz primerjave velikostnih porazdelitev veziklov in njihovega števila v posameznih mozaikih lahko ugotovimo, kako je dodani aditiv vplival na številnost in morfologijo veziklov v populaciji skozi čas. V raziskavi smo analizirali eksperimenta z dvema različnima aditivoma, fulereni (nanodelci C_{60}) in pozitivno nabitimi ter nevtralnimi kobalt-feritnimi nanodelci ($CoFe_2O_4$).



Slika 9 (a) Povprečen premer sferičnih veziklov v kontrolni (C) populaciji ob času 0 in po 90 minutah ter v populacijah z negativno nabitimi (CF-CA) in nevtralnimi (CF) kobalt-feritnimi nanodelci po 90 minutah inkubacije. (b) Število nesferičnih veziklov in (c) število verižic v C, CF in CF-CA populacijah ob časovnem obdobju 0 in po 90 minutah inkubacije z ali brez nanodelcev.

Lipidni vezikli in kobalt-feritni nanodelci ($CoFe_2O_4$)

V poskusu s kobalt-feritnimi nanodelci je bilo iz štirih mozaikov segmentiranih 9781 veziklov vseh oblik. Tukaj so bile opazovane kontrolna populacija (C) in populaciji izpostavljeni negativno nabitim (CF-CA) in nevtralnim (CF) kobalt-feritnimi nanodelcem. Primerjava velikosti sferičnih veziklov med populacijami je pokazala, da se je povprečen premer veziklov v neizpostavljeni kontrolni populaciji po 90 minutah inkubacije zmanjšal s 6,5 μm na 6 μm (slika 9a). V populacijah, izpostavljenih nevtralnim in negativno nabitim kobalt-feritnim nanodelcem, so se premeri veziklov v povprečju povečali na 8,1 μm oziroma 8,5 μm (slika 9a). Prav tako smo ugotovili povečano pojavljanje nesferičnih veziklov (5-15 % vseh) v populacijah z dodanimi kobalt-feritnimi nanodelci (slika 9b). Najbolj opazno je pojavljanje verižic, ki je desetkrat večje v populacijah, izpostavljenim negativno nabitim $CoFe_2O_4$ nanodelcem (slika 9c).

Lipidni vezikli in C_{60} nanodelci

V eksperimentu z nanodelci C_{60} je bilo segmentiranih 7670 veziklov v 810 mikrografijah. Kot je predstavljeno v tabeli 1, so bile tukaj opazovane tri populacije: kontrolna (z dodano glukozno raztopino), referenčna (z dodanim $ZnCl_2$) in nano (z dodanim C_{60}). Ugotovili smo, da je učinek C_{60} takojšen in da tako kot referenčna kemikalija $ZnCl_2$ pospeši pokanje veziklov. Najbolj opazen je učinek blizu mesta dodajanja aditiva (P1 na sliki 2), kjer je v nano in referenčni populaciji popokalo 80 % veziklov (slika 10).

Na drugi sledi snemanja, nekaj milimetrov oddaljenem od lokacije dodajanja aditiva, je bil učinek C_{60} manjši od tistega pri $ZnCl_2$, spremembe pa so bile opazne šele po 100 minutah inkubacije (slika 10).

Ugotovljen vpliv nanodelcev na vezikle

Pridobljeni rezultati kažejo, da imata testirani koncentraciji tako C_{60} kot tudi detergenta $ZnCl_2$ vpliv na lipidne vezikle. V večini primerov povzročita pokanje veziklov večjih dimenzij. Morfološke spremembe so se pokazale v primeru dodajanja nanodelcev $CoFe_2O_4$, kjer smo ugotovili povečano pojavljanje nesferičnih veziklov, najbolj opazno verižic.

Z rezultati eksperimentov smo pokazali uporabnost metodologije (kombinacije eksperimentalnega protokola, korakov računalniškega procesiranja slik in analize pridobljenih podatkov) za ugotavljanje vpliva nanodelcev na populacije lipidnih veziklov. Vzorec tisočih veziklov je dovolj velik, da smo zajeli tudi statistično zadosti velik delež veziklov, na katerega so nanodelci vplivali. Z opazovanjem malih vzorcev (desetine veziklov) zaznanih sprememb namreč ni mogoče ločiti od normalne morfološke variabilnosti populacij veziklov.

Lepljenje videoposnetkov v mozaike in avtomatska segmentacija veziklov zagotavljata visoko stopnjo zaupanja v rezultate. Prednost metode je tudi, da je bistveno bolj časovno ugodna za raziskovalce. Pred avtomatizacijo je obdelava mikrografij zahtevala zelo obsežno ročno delo, ki smo ga s predstavljenim pristopom avtomatske segmentacije zmanjšali tudi do osemkrat. V večini primerov lahko operater zdaj že v enem dnevu dobi rezultate, za kakršne je bil prej potreben en teden ročnega dela.

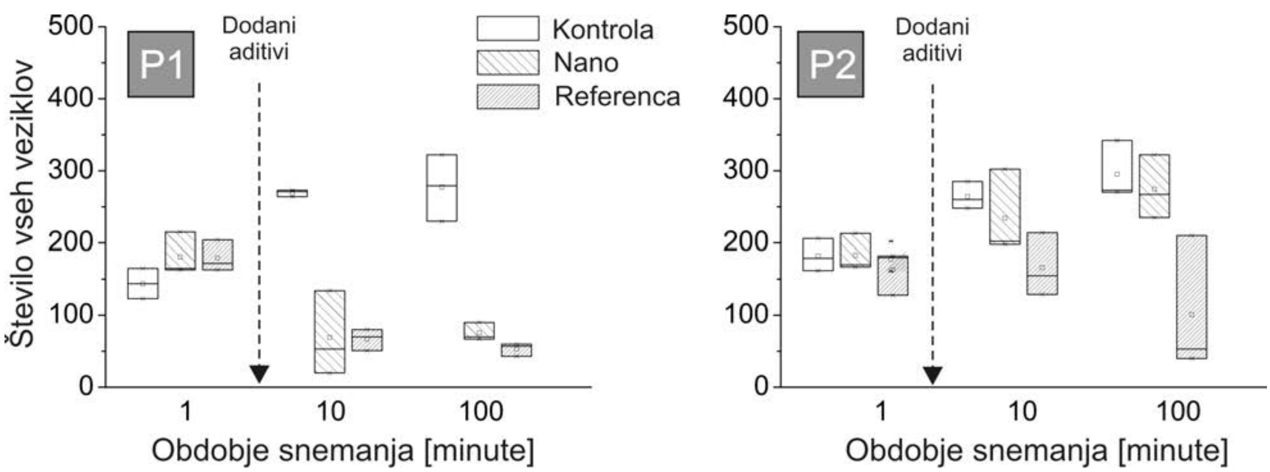
Zaključek

Avtomatiziran pristop pri zajemu in obdelavi slik lipidnih veziklov omogoča analizo tisočih veziklov. To je zadosti velika populacija, da lahko pridobimo zanesljive statistično podprte rezultate o njihovih morfoloških spremembah kljub raznolikosti populacij veziklov samih. Rezultati analize populacije veziklov so potrdili predpostavko o vplivu nanodelcev na lipidne membrane.

Postavljena metodologija in z njo pridobljeni rezultati so doprinos k razumevanju interakcij med membranami in nanodelci. Kažejo, da imajo slednji potencial, da vplivajo na lipidno komponento biološke membrane. Te ugotovitve so v skladu z domnevami o nano-specifičnem biološkem učinku nanodelcev.[29]

Zahvala

Raziskovanje je bilo delno podprto s strani ARRS kot status mladega raziskovalca Jerneja Zupanca.



Slika 10 Število vseh veziklov na mestu snemanja (P1) bližje dodajanju aditivov: kontrolna (z dodano glukozno raztopino), referenčna (z dodanim $ZnCl_2$) in nano (z dodanim C_{60}) populacija. Število je podano pred dodajanjem (obdobje 1) in po dodajanju nanodelcev ali referenčne kemikalije (obdobje po 10 in po 100 minutah). Opazno je zmanjšanje števila veziklov v nano in referenčni populaciji takoj po dodajanju aditiva. Desni graf: podobno kot P1, vendar na mestu P2, ki je dlje stran od dodajanja aditiva. Tukaj učinek nanodelcev ni bil tako opazen, referenčna kemikalija pa je zmanjšala število veziklov šele po obdobju 100 minut inkubacije. Na obeh grafih je s puščico nakazan čas, ko sta bila dodana aditiva.

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Izvirni znanstveni članek ■

Napredne glasovne e-storitve v zdravstvu

Jerneja Žganec Gros, Tomaž Domajnko, Tanja Majcen, Marko Ivančič, Aleš Mihelič, Žiga Golob, Primož Jakopin, Petar Brajak, Nataša Planinc

Izvleček. V članku predstavljamo dosežke projekta ZEN (zdravstvene e-storitve z naprednimi glasovnimi uporabniškimi vmesniki). S pomočjo sinteze slovenskega govora smo razvili prototip e-storitve za podporo pri jemanju zdravil s poudarkom na ostarelih uporabnikih ter uporabnikih s posebnimi potrebami, predvsem slepih in slabovidnih. Storitev uporabnikom preko set-top box-a ali mobilnega telefona omogoča vpogled v seznam zdravil, ki so jim predpisana, v podatke o posameznih predpisih, kot tudi v navodila zdravil. Poleg tega storitev s pomočjo glasovnih in besedilnih sporočil opominja uporabnika, da mora vzeti predpisani odmerek zdravil. Podajamo rezultate evalvacije nove storitve.

Advanced Voice-enabled e-Health Services

Abstract. We present how Slovenian text-to-speech synthesis technologies have been used to develop a prototype solution of a novel e-health service called ZEN, which will focus on the elderly, along with blind and visually impaired users. The service features two communication channels for delivering information to the users: via telephone and via a TV screen, connected to a set-top-box. The user can browse and listen to descriptions of prescribed medicines and therapies, and receive textual and/or visual reminders related to the therapy. The results of an evaluation study are presented.

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Uvod

V sodobni družbi je zagotavljanje sistema zdravstvenega varstva kritičnega pomena, saj med drugim predstavlja merilo za demokratično razvitost družbe. Za njegovo uspešno delovanje je potrebno vzpostaviti učinkovit način sodelovanja in nadzora med vsemi vpletenimi v celotni verigi zdravstvenega varstva.

Pomemben del interakcije človeka s strojem je *uporabniška izkušnja*, ki v večini primerov predstavlja bistven kriterij za odločitev o posvojitvi in redni uporabi nove naprave ali e-storitve s strani končnih uporabnikov. Izhodiščna predpostavka projekta je bila, da uvedba glasovnega uporabniškega vmesnika lahko pomembno doprinese k izboljšanju uporabniške izkušnje v zdravstvenih e-storitvah. Da bi to preverili, smo razvili celotno verigo tehnoloških komponent pri vzpostavitvi zdravstvene e-storitve za izbrano zdravstveno situacijo ter ugotavljali spremembe v uporabniški izkušnji ob dodatku naprednega glasovnega uporabniškega vmesnika.

Namen projekta *ZEN: zdravstvene e-storitve z naprednimi glasovnimi uporabniškimi vmesniki* je bila zasnova nove e-storitve na področju e-vključenosti in e-zdravja ter interdisciplinarni predkonkurenčni razvoj informacijsko-komunikacijskega sistema, podprtega z naprednimi glasovnimi uporabniškimi vmesniki. Poglavitno pozornost smo posvetili razvoju in validaciji novih tehnoloških rešitev v zdravstvenih e-storitvah, ki povečujejo uporabniško izkušnjo pri uporabi tovrstnih storitev.

Pri izdelavi demonstracijskega prototipa ZEN smo uporabili dolgoletne izkušnje vseh projektnih partnerjev iz področij razvoja govornih tehnologij (Alpineon) in jezikovnih tehnologij (Inštitut za slovenski jezik v okviru ZRC-SAZU), informacijskih tehnologij v zdravstvu (SRC d.o.o.) ter odprtokodnih komunikacijskih tehnologij (Medius d.o.o.). V okviru projekta smo razvili nove jezikovne vire (referenčni slovar izgovarjav), številne nove tehnološke rešitve (glasovni strežnik, podatkovno-komunikacijski strežnik, glasovno-podprta aplikacija za set-top box) ter novo odprtokodno tehnološko rešitev (odprtokodni TK strežnik za konvergentno povezovanje spletnih zdravstvenih e-storitev in govornih tehnologij).

V fazi integracije smo razvite tehnološke rešitve integrirali v enovit demonstracijski prototip, ki ga je možno prilagoditi za številne primer uporabe. Rezultate projekta je preveril zunanji recenzor. Ocenila jih je tudi skupina končnih uporabnikov rezultatov projekta – ostareli ter slepe in slabovidne osebe, ki so preverjali tako primernost uporabe glasovnih uporabniških vmesnikov v zdravstvenih e-storitvah, kot tudi primernost izvedbe celotne rešitve na demonstriranem primeru uporabe v okviru Festivala za tretje življenjsko obdobje 2010.

Glasovne tehnologije

Govor predstavlja najnaravnejši način komunikacije med človekom in strojem[1]. Govorno podprti uporabniški vmesniki omogočajo uporabniško prijazno komunikacijo, še posebej v okolju mobilnih komunikacij. Ponujajo tudi možnost enakopravnega vključevanja skupin oseb s posebnimi potrebami, predvsem ostarelih, slepih in slabovidnih v sodobno informacijsko družbo. Sistemi, ki vključujejo govorne tehnologije, omogočajo hitre odzivne čase, znižujejo stroške poslovanja in prispevajo k večji prepoznavnosti na trgu. Nudijo možnost avtomatizacije obstoječih storitev in cenenega razvoja množice novih storitev in naprav na številnih sektorjih uporabe.

Za uspešen razvoj in uporabo govorno podprtih rešitev je potrebno zagotoviti učinkovite in visoko kakovostne komponente sistema govornega dialoga, to je uspešnost avtomatskega razpoznavanja govora in kvalitetno, razumljivo in naravno zveneče sintezo govora, ki omogoča samodejno pretvarjanje vhodnih besedil v glasovno obliko.[2]

Raziskave in razvoj na področju govornih tehnologij se danes hitro prenašajo v komercialne sisteme, ki postajajo vse bolj razširjeni. Za jezike s široko bazo govorcev se rešitve samodejne prepoznave govora (angl. automatic speech recognition ali ASR) in samodejne sinteze govora (angl. text-to-speech synthesis ali TTS) vgrajujejo v cenovno ugodne programske pakete, namenjene predvsem uporabi na osebnih računalnikih.[3,4] Evropa danes predstavlja enega najnaprednejših trgov govornih tehnologij. Evropska unija si prizadeva, da so potrebna orodja in viri na razpolago za vse jezike Evropske unije kot tudi glavne svetovne komercialne jezike, s čimer utira pot prodorni več jezikovni informacijski evropski družbi. Z uvajanjem večjezičnih proizvodov in storitev poskuša Evropska Komisija doseči svoj ambiciozni cilj – posplošitev dostopa do informacij za vse evropske državljane, ki je tudi ključni cilj pobude *i2010*.

Vendar se obseg sistematične raziskanosti jezikov, ki se govorijo v Evropi, od enega jezika do drugega zelo razlikuje, pri čemer je bila v sklopu posebnih projektov znotraj EU, pa tudi nacionalnih in komercialnih projektov, dobro raziskana le peščica jezikov (angleščina, španščina, francoščina in nemščina), nekateri pa so bili komajda obravnavani. Pogosto so bile prav nove države članice tiste, ki niso imele možnosti za razvoj jezikovnih tehnologij za svoje pisne in govorjene jezike. Za slovenski jezik je na voljo komercialno dostopen prepoznavalnik govora za omejeno področje uporabe ter več raziskovalnih prototipov.

Sinteza govora predstavlja postopek samodejnega pretvarjanja vhodnih besedil, zapisanih v elektronski obliki, v govor. Za slovenščino sicer obstaja več sintetizatorjev govora, ki so namenjeni uporabi na osebnih računalnikih.[5] Ni pa na voljo robustne in razširljive strežniške rešitve, ki bi ponujala usluge sinteze govora v širokemu spektru e-storitev in aplikacij. Prav ta tehnološka rešitev je bila razvita v okviru projekta ZEN. Izboljšan je bil tudi del sintetizatorja govora, ki določa izgovarjavo novih, neznanih besed, kar je še zlasti pomembno pri vključevanju sinteze govora na novo področje uporabe. Razširjen je bil tudi slovar izgovarjav, ki sedaj pokriva vse iztočnice iz Slovenskega pravopisa.

Opis e-storitve ZEN

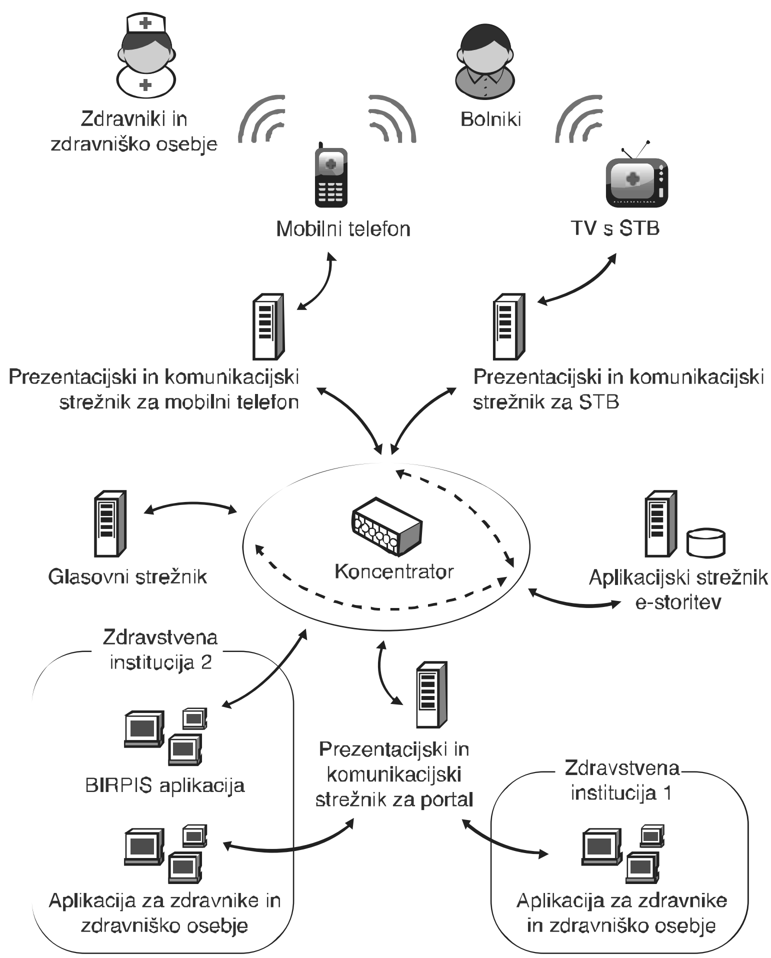
Pomemben del interakcije človeka s strojem je *uporabniška izkušnja*, ki v večini primerov predstavlja bistven kriterij za odločitev o posvojitvi in redni uporabi nove naprave ali e-storitve s strani končnih uporabnikov. V okviru projekta smo razvili celotno verigo tehnoloških komponent pri vzpostavitvi značilne zdravstvene e-storitve ter ugotavljali spremembe v uporabniški izkušnji ob dodatku naprednega glasovnega uporabniškega vmesnika.

Zdravstvena e-storitev z naprednimi uporabniškimi vmesniki – ZEN – je namenjena spremljanju pacientovega stanja in poteka zdravljenja na daljavo. Predstavlja pripomoček pri izvajanju poteka zdravljenja. Uporabniku lahko služi kot opomnik za redno izvajanje aktivnosti, predpisanih s strani zdravnika, ter kot informator in podatkovni posredovalec med njim ter zdravnikom oz. zdravstvenim osebjem.

V sistemu ZEN se podatki uporabniku lahko posredujejo preko dveh komunikacijskih kanalov. Prvi je telefonski kanal, kjer uporabnik dostopa do informacij v obliki glasovnega dialoga, podprtega s sintetizatorjem govora, ki govor samodejno generira iz dinamičnega elektronskega besedila.

Drugi komunikacijski kanal predstavlja set-top box (STB), kjer v dialogu z uporabnikom poleg glasovnih komponent nastopajo še vizualno grafične, kot so npr. prikaz besedila prilagodljive velikosti, slike, ipd.

Preko istih dveh komunikacijskih kanalov lahko tudi uporabnik sproži zahtevo za izvajanje e-storitve.



Slika 1 Osnovna arhitektura sistema ZEN.

Arhitektura sistema ZEN

Sistemska arhitektura ZEN modulov, ki smo jih razvili v okviru projekta, je predstavljena na sliki 1. Poglavitni moduli sistema so naslednji: podatkovno-komunikacijski strežnik, TK strežnik, glasovni strežnik in aplikacija za STB napravo.

Podatkovno-komunikacijski strežnik

Podatkovno-komunikacijski strežnik, glede na nastavitve, in podatke, ki jih sistem ZEN želi posredovati uporabniku, določi tip dialoga in komunikacijski kanal. Skrbi za podatke, ki so potrebni za ustvarjanje dinamičnih dialogov z uporabnikom za komunikacijo preko STB naprave. Dialogi poleg glasovnih vsebujejo tudi vizualno-grafične elemente. Način prikaza podatkov lahko uporabnik spreminja glede na svoje potrebe. Velikost na ekranu prikazanega besedila je nastavljiva, kar je primerno za starejše ter slabovidne. Podatki se med sistemom in STB napravo prenašajo preko varnega šifriranega kanala.

Vsi podatki o poteku zdravljenja, predpisanih zdravilih ipd., se hranijo na podatkovno-komunikacijskem strežniku v šifrirani obliki. Do njih ima dostop samo pooblaščeno medicinsko osebje ter, v določeni obliki in obsegu, pacient. Podatke sistem pacientu posreduje preko dveh kanalov: preko STB naprave ter preko telefonskega kanala.

Aplikacija za zdravstveno osebje lečečemu zdravniku in ostalemu pooblaščenemu zdravstvenemu osebju omogoča spremljanje poteka pacientovega zdravljenja na daljavo, vpisovanje in spreminjanje podatkov o zdravljenju, predpisanih zdravilih, časovnih intervalih zaužitja zdravila ter drugih s pacientovim zdravljenjem povezanih podatkih. Vsi ti podatki se zapisujejo v podatkovno zbirko na podatkovno-komunikacijskem strežniku.

TK strežnik

Skrbi za ustvarjanje dialogov z uporabnikom za komunikacijo preko telefonskega kanala. Odvisen je od podatkovno-komunikacijskega strežnika, od katerega prejema zahteve po ustvarjanju dialoga z uporabnikom ter podatke, ki jih mora le temu posredovati. V domeni TK strežnika so govorni dialogi, ki potekajo preko telefonskega govornega kanala, za razliko od dialogov, ki so namenjeni komunikaciji preko STB naprave in vsebujejo tudi vizualno grafične elemente. V smeri od sistema proti pacientu poteka pretok informacij v obliki sintetiziranega govora, v obratni smeri pa preko detekcije pritiska tipk (DTMF) ali snemanja glasovnega sporočila.

Rešitev je bila izvedena na podlagi odprtokodne platforme SDP (Service Delivery Platform) in konceptov okolij IMS (IP Multimedia Subsystem) in omogoča integracijo spletnih storitev z govorno telefonijo (klasična stacionarna telefonija, mobilna telefonija, VoIP, SoftPhone).

Arhitektura je zgrajena na osnovi najboljših odprtokodnih orodij in tehnologij za SDP in na ta način zagotavlja dolgoročno odprtost rešitev, hiter razvojni cikel, prilagoditev novim produktom in standardom ter nizko ceno. Arhitektura je zasnovana na konceptih SOA (Service Oriented Architecture) in zajema celoten sklad komponent, od operacijskega sistema do vmesnikov, ki omogočajo:

- pošiljanje individualiziranih opomnikov,
- snemanje in pošiljanje glasovnih sporočil,
- objave posnetkov telefonskega govora,
- sintezo govora iz obvestil na oglasni deski s pomočjo glasovnega strežnika,
- integracijo storitev s koledarji.

Glasovni strežnik

Glasovni strežnik skrbi za pretvorbo elektronskega besedila v govor. Vsi dialogi, ki predvidevajo komunikacijo z bolnikom oz. posredovanje podatkov preko govornega dialoga, uporabljajo glasovni strežnik za dinamično sprotno tvorjenje govora iz podatkov, ki so shranjeni v sistemu v obliki elektronskega besedila. Klientom dodeljuje kanale za sintezo ter druge potrebne vire.

Strežnik skrbi za identifikacijo pošiljatelja zahteve za sintezo govora iz elektronskega besedila. Iniciatorji zahtevka so lahko ostali strežniki sistema ZEN ali neposredno STB naprave. Identifikacijo lahko izvede glede na nameščeno serijsko številko, IP naslov ali nameščen certifikat za varno šifrirano komunikacijo). Glasovni strežnik skrbi tudi za upravljanje s profili uporabnikov in vodi statistiko po uporabnikih. Zaradi hitrejšega odziva je sposoben tudi hraniti v govor že pretvorjena sintetizirana besedila (posebno v primeru vnaprej definiranih dialogov, navodil ipd.) v obliki zvočnih datotek. Prav tako skrbi za pretvorbo vhodnega besedila (SSML – W3C Speech Synthesis Markup Language) v format, primeren za pretvorbo v govor.

V okviru projekta je bil tudi nadgrajen modul za grafemsko-fonetično pretvorbo vhodnih besedil ter zgrajen nov slovar izgovarjav za preko 90.000 iztočnic iz Slovenskega pravopisa.[6] Izgradnja slovarja je temeljila na formatu slovarja izgovarjav SI-PRON.[7]

Slika 2 Primeri posnetkov zaslona uporabniškega vmesnika ZEN.

Podatki in komunikacija med moduli

Vsi podatki se shranjujejo na podatkovno-komunikacijskem strežniku v šifrirani obliki. Do njih lahko dostopa samo pooblaščeno zdravstveno osebje. Dostop do svojih podatkov, v vnaprej določenem obsegu in obliki, pa ima tudi pacient/uporabnik. Podatki se na pacientovo zahtevo pretvorijo v obliko primerno za izbrani tip komunikacijskega kanala in dialoga ter se posredujejo pacientu na STB ali telefon.

Komunikacija med moduli v sistemu (med napravo STB ter podatkovno-komunikacijskim strežnikom, med aplikacijo za zdravstveno osebje ter podatkovno-komunikacijskim strežnikom) poteka preko varnih šifriranih kanalov. Podatki so med prenosom zaščiteni pred vpogledom tretjih oseb. Sistem je sposoben zagotoviti vzpostavitev varnega kanala ne glede na pot prenosa podatkov (preusmeritve, podomrežja, usmerjevalniki in druge namenske naprave). Identifikacija uporabnika temelji na osnovi nameščene serijske številke, uporabnikovega certifikata ter IP oz. MAC naslova.

Komunikacija z uporabnikom

Kot rečeno, sta v sistemu ZEN sta za komunikacijo sistema oz. zdravstvenega osebja s pacientom predvidena dva komunikacijska kanala: STB ter telefon.

STB je naprava, namenjena priklopu na televizor oz. monitor. Pacient jo krmili s pomočjo daljinskega upravljalnika in preko nje dostopa do različnih podatkov v zvezi z zdravljenjem. Naprava podatke pacientu posreduje v slikovni in/ali zvočni obliki. Prav tako pacientu omogoča posredno oz. neposredno komunikacijo z zdravstvenim osebjem, deluje pa tudi kot pripomoček za spremljanje dnevnega izvajanja zdravljenja - tako količinsko kot časovno. Primer uporabniškega vmesnika ZEN je prikazan na sliki 2. Pacienta opozarja na termin bližajoče se aktivnosti zdravljenja, in od njega pričakuje tudi potrditev o izvedeni aktivnosti.

Telefon predstavlja alternativni komunikacijski kanal za posredovanje informacij v obe smeri. Komunikacija poteka preko govorjenega dialoga (v smeri k pacientu) oz. pritiska tipk na telefonskem aparatu (v smeri od pacienta) in za razliko od STB ne vsebuje vizualno grafičnih elementov.

Značilni scenariji uporabe e-storitve ZEN

Uporabnik lahko preko e-storitve ZEN prejema sporočila od zdravnika, vezana na dnevno spremljanje poteka zdravljenja, prejema opozorila na bližajoči se ali spuščen termin za izvajanje določene aktivnosti, povezane z zdravljenjem (denimo redno razgibavanje ali jemanje zdravil), zdravnik lahko od svojega pacienta zahteva potrditev o izvedeni aktivnosti ipd.

Pacient lahko preko e-storitve dostopa do rednih napotkov svojega zdravnika, do opisov predpisanih zdravil (navodila, stranski učinki, doze, trajanje, količine…), lahko posredno ali neposredno komunicira z lečečim zdravnikom oz. zdravstvenim osebjem, lahko zaprosi za dodatne informacije v zvezi z zdravljenjem ali preveri, kdaj je nazadnje izvedel predpisano aktivnost v zdravljenju.

Primer 1: Zdravnik ureja koledarje za svoje paciente (npr. datumi in ure za predpisano jemanje zdravil, opomniki in obvestila). Vsakemu dogodku zdravnik na portalu lahko pripne informacijo bodisi v obliki besedila ali govornega sporočila.

Sistem ob uri, ki je določena s koledarjem kontaktira pacienta, bodisi preko STB, bodisi preko telefonskega kanala, in ga obvesti o terminu predpisane aktivnosti v poteku zdravljenja. Pacient lahko sistemu potrdi izvajanje dejavnosti preko istega komunikacijskega kanala.

Primer 2: Pacient iz Primera 1 se ne more spomniti, ali je ob predpisani uri izvedel razgibavanje ali ne. S pomočjo e-storitve ZEN se prepriča o dejanskem stanju.

Primer 3: Zdravnik na oglasni deski svojih pacientov pušča redna obvestila (navodila, informacije o vrsti in napredku zdravljenja, informacije o predpisanih zdravilih, termin pregleda pri zdravniku) v obliki besedila ali govornega sporočila. Pacient preverja obvestila preko e-storitve ZEN. Slepi in slabovidni uporabnik se lahko odloči za sprejem sporočila v glasovni obliki.

Evalvacija sistema

V fazi integracije smo razvite tehnološke rešitve integrirali v enovit demonstracijski prototip, ki ga je možno prilagoditi za številne primer uporabe.

Posebej smo ročno evalvirali nove jezikovne vire. Samodejna grafemsko-fonetična transkripcija iztočnic iz Slovenskega pravopisa namreč ni bila vedno uspešna.[8]

K preskusu nove e-storitve ZEN smo povabili zunanjega recenzorja in skupino končnih uporabnikov rezultatov projekta – ostarele ter slepe in slabovidne osebe. V nadaljevanju podajamo rezultate obeh evalvacij.

Evalvacija s strani končnih uporabnikov

Med prvimi testnimi uporabniki prototipa je bila skupina predvidenih končnih uporabnikov rezultatov projekta – ostareli ter slepe in slabovidne osebe, ki so preverjali tako primernost uporabe glasovnih uporabniških vmesnikov v zdravstvenih e-storitvah, kot tudi primernost izvedbe celotne rešitve na demonstriranem primeru uporabe v okviru *Festivala za tretje življenjsko obdobje 2010*. Na istem Festivalu smo leto poprej zbirali uporabniške zahteve za e-storitev ZEN.

Sestavili smo anketo, ki je obsegala 6 vprašanj. Vprašanja so se nanašala na opremljenost bivalnih prostorov anketirancev z informacijsko komunikacijsko opremo, njihove potrebe po dostopu do zdravstvenih storitev ter na ocenjevanje bistvenih vidikov uporabnosti e-storitve ZEN.

Anketiranih je bilo 60 obiskovalcev festivala F3ŽO 2010. Vsem anketirancem je bila najprej predstavljena razvita aplikacija za dostop do e-zdravstvenih storitev, nato so izpolnjevali anketo.

- Večino anketirancev so predstavljali starejši (52 % anketirancev je bilo starejših od 64 let, 47 % pa starih med 20 in 64 let); 75 % anketirancev je bilo ženskega spola.

- Vsi anketiranci so imeli dostop do tv sprejemnika ter telefona. Telefon uporablja pogosto ali zelo pogosto več kot 63 % anketirancev, vsi izmed njih pa so že uporabljali telefon.

- Veliki večini (78 %) anketirancev se zdi koristno, da bi bili na bližajoč termin za obisk zdravnika opozorjeni preko telefona ali tv sprejemnika. Enako vprašanje smo zastavili tudi pri zbiranju uporabniških zahtev na istem festivalu eno leto pred evalvacijo, ko smo dobili praktično enake rezultate.

- Anketirance smo vprašali, ali se jim zdi koristno, da bi lahko nasvete zdravnika enostavno preverili v tekstovni ali v glasovni obliki preko tv sprejemnika oz. v glasovni obliki preko telefona. Enako vprašanje smo postavili tudi pri zbiranju uporabniških zahtev. Anketirancem se je v tej anketi zdelo takšno preverjanje precej bolj koristno. Kar 92 % anketirancem se je zdelo primerno preverjanje informacij na tv sprejemniku v tekstovni obliki, kar je več kot 20 % več v primerjavi s prejšnjo anketo. Preverjanje v glasovni obliki preko tv sprejemnika se je zdelo koristno 84 % anketirancem (v prejšnji anketi 62 %), v glasovni obliki preko telefona pa 86 % anketirancem (v prejšnji anketi 77 %). Vzrok za porast deleža anketirancev, ki se jim zdi tako preverjanje informacij koristno, je najverjetneje v tem, da so si ljudje pred demonstracijo e-storitve ZEN težko predstavljali, na kakšen način bi lahko takšne informacije preverjali preko domačega tv sprejemnika.

- Anketiranci so ocenjevali tudi različne vidike razvite aplikacije, kot so berljivost, razločnost, hitrost govora, možnost prekinitve, prijaznost navigacije ter uporabnost sistema. Anketiranci so vse vidike aplikacije večinoma ocenili kot dobre ali odlične, izrazili pa so tudi željo po možnosti prekinitve glasovnega predvajanja. Posebej lahko izpostavimo odgovore na vprašanje o uporabnosti e-storitve ZEN, na katerega je odgovorilo 97 % anketirancev, od katerih storitve nihče ni označil kot slabe, 9 % jo je označilo kot zadovoljivo, 46 % kot dobro in 45 % kot odlično.

Evalvacija s strani zunanjega recenzorja

Rezultate projekta je preveril tudi zunanji recenzor z vidika doseganja ciljev projekta, kot tudi s tehniško-uporabniških vidikov projekta. V tabeli 1 podajamo rezultate te recenzorske ocene.

Tabela 1 Rezultati ocen tehniško-uporabniških vidikov glasovno podprte e-storitve ZEN na štiristopenjski lestvici (1 pomeni najnižjo, 4 pa najvišjo stopnjo kakovosti).

Kriterij	Ocena	Opis kriterija
Interoperabilnost in standardi	4	Zagotavljanje interoperabilnosti in uporaba odprtih standardov
Namestitev/priprava za uporabo	*	Preprostost/kompleksnost/samodejnost/trajanje namestitvenega postopka…
Stopnja informacijske varnosti	4	Prenos, dostopnost in zaščita podatkov
Kvaliteta govornega up. vmesnika	4	Avtomatska sinteza govora
Berljivost in jasnost besedila	4	Uporaba barv, pisav, kontrastov, …
Uporabnost	4	Preprostost/kompleksnost sistema za končnega uporabnika rešitve
Navigacija	4	Preprostost navigacije po menijih, informacija o trenutnem meniju

* Ocena ni možna.

Zaključek

V okviru projekta ZEN smo izvedli raziskave s področja razvoja na storitvah temelječih rešitev za podporo sodelovanja ponudnikov in uporabnikov storitev zdravstvenega varstva z namenom povečanja dostopnosti, uporabe, prijaznosti do uporabnika in preglednosti storitev z zdravstvenega področja. Pokazali smo primernost uporabe govornih tehnologij v zdravstvenih e-storitvah.

Z vključitvijo govornega kanala in televizorja ter telefona kot dostavnega kanala sistem ZEN dosega ciljno populacijo v veliko večji meri kot druge informacijske rešitve. To namreč predstavlja poenostavitev uporabe informacijske tehnologije s stališča ciljne populacije – praviloma starejšega, gibalno in informacijsko podrejenega segmenta prebivalstva. Takšna zasnova omogoča izboljšanje dosega informacijskih rešitev v ciljni populaciji in zagotavlja platformo, na kateri bo mogoče v prihodnosti razviti in ponuditi širok nabor informacijsko temelječih storitev, ki bodo dopolnjevale realne zdravstvene e-storitve.

Zahvala

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Research Paper ■

A Double-blind Placebo-controlled Cross-over Study on the Effects of Botulinum Toxin Type A on Upper Limb Disorders

Jelka Janša, Dejan Georgiev, Lidija Ocepek, Zvezdan Pirtošek, Gaj Vidmar

Abstract. Botulinum treatment has been proven to be a promising treatment for many dystonic and spastic disorders. Apart from correction of posture and pain relief, functional testing is an important part of pre - and post-treatment assessment. We report results and dilemmas of using two assessment scales in a double-blind, placebo-controlled cross-over study on 10 patients with upper limb motor disorders. While the improvement on the Arm Function Test (AFT) after the Botulinum session was not statistically significantly higher than after placebo, the difference in favour of the treatment was much more evident on the 0-5 self-assessment scale. We believe that AFT is not sufficiently sensitive or at least not superior to simpler global scales, and that measurement of focal disability does not entirely clarify functional changes after treatment with Botulinum Toxin.

Dvojno slepa kontrolirana navzkrižna študija učinkov botulina A na bolezni zgornjih udov

Izvleček. Zdravljenje z botulinom se je uveljavilo pri razčinih boleznih z distonijo ali spastičnostjo. Poleg izboljšanja drže in lajšanja bolečine je funkcijsko testiranje poemmben vidik ocenjevanja izida zdravljenja. Poročamo o rezultatih in dilemah pri dveh ocenjevalnih lestvicah, ki smo jih uporabili v dvojno slepi s placebom kontrolirani navzkrižni študiji na 10 pacientih z gibalnimi boleznimi zgornjih udov. Izboljšanje na funkcijskem testu roke (AFT) po zdravljenju ni bilo statistično značilno večje v primerjavi s placebom, razlika v prid zdravljenja pa je bila mnogo jasnejša na samoocenjevalni lestvici 0-5. Menimo, da AFT ni dovolj občutljiv oziroma ni ustreznejši od preprostejših globalnih lestivc, ter da merjenje lokalnih zmanjšanih zmožnosti ne razjasni vseh funkcijskih sprememb po zdravljenju z botulinom.

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Introduction

Botulinum toxin (BTX) is one of the most potent neurotoxins known. It is a microbial protein that exists in several serotypes, from A to G.[1] For now, two antigenically distinct serotipes (BTX-A in BTX-B) are available for clinical practice.[2] BTX acts as enzyme at the presynaptic membrane to cleave three polypeptides that are essential for exocytosis (synaptosomal associated protein SNAP-25, vesicle associated protein – VAMP, and syntaxin). Different BTX types cleave different polypeptides and block acetylcholine release at the neuromuscular junction, which is in turn responsible for its therapeutic action to relive dystonia, spasticity and related disorders.

Recently, three review articles explored the efficacy of BTX therapy in different neurological conditions. The authors concluded that it is efficient therapy for cervical dystonia; probably effective in the treatment of focal limb dystonia, laryngeal dystonia, blepharospasm and tremor; and possibly effective in the treatment of hemifacial spasm.[3] It is also an effective in the treatment of spasticity.[1] However, there is controversy about its efficacy in the treatment of autonomic disorders and pain syndromes.[4]

Most of the existing studies on the efficiency of BTX therapy addressed the question of clinical improvement of the muscle tone as defined by reduction of spasticity or dystonia in patients.[5] There are some studies that showed inconsistent functional benefits from the therapy.[6,7] However, the functional consequences of the therapy remain unclear despite the fact that the functional issues are often a major focus of the rehabilitation programmes,[8] which are usually complex and include many different elements.[9]

Upper limb abilities presented by patients with disabled upper extremity can be divided into passive and active functions. Passive functions relate to the tasks preformed by the non-affected arm, whereas active functions include tasks that the subject performs with the affected limb.[8] Active function can be actually seen at as the capacity to move the body or its parts actively and can range from simple active movements to a complex movements and even more complex actions.[10]

As already mentioned, besides the clinical improvement the treatment with BTX also implies functional improvement. The functional goals include improvement of active and passive function, reduction of pain associated with passive mobilisation (in post-stroke patients) and painful spasms, improvement of hygiene, and prevention of contractures.[11] Consequently, estimation of functional outcome after BTX therapy is very important, and it might be actually more important than the clinical improvement itself.[12] One other important point is the sensitivity and specificity of functional tests used in assessment of the functional state of the upper extremity after BTX therapy.[13,14]

We present a double-blind placebo-controlled cross-over study that focused on the functional improvement after the BTX therapy measured by the medical professionals, as well as on the impact of the therapy from the patients' personal perspective. Patients with spasticity and/or dystonia of different aetiology were included, because the aim of the study was to test the functional efficacy of BTX therapy regardless of the cause of the treated condition.

Methods

Subjects

Ten patients with upper limb motor impairment, spasticity and/or dystonia, after stroke, encephalitis or cerebral palsy (six male and four female) were included in the study. Each patient gave an informed consent before entering the study.

Assessment tools

Two assessment scales were used: Arm Function Test (AFT)[14] and Self-assessment of Functional Improvement (SAFI). The former evaluates functional ability of the affected arm using seven graded tasks: (1) Use both hands to open jar; (2) Use both hands to rule a line; (3) Use affected hand to pick up and release 5 cm cylinder; (4) Use affected hand to pick up and release 1.25 cm cylinder; (5) Use affected hand to drink water from glass; (6) Use affected hand to comb hair; (7) Use affected hand to open and close clothes peg. Every task is scored either as 1 (capable of execution) or 0 (incapable of execution), so the overall score range is 0-7. The later test is a subjective self-assessment tool of functional improvement which quantifies the patient's perception of changes in the functional status of the affected hand. The 6-point scale is: (0) no functional improvement, (1) insufficient functional improvement, intermediate grades (2, 3, 4), (5) excellent functional improvement. The patients' response on this scale is assumed to show a faithful representation of their own perceptions of change in hand function.

Botulinum Toxin

BTX-A (Dysport) was used in the study: 500 units (U) of Dysport were diluted in 1 ml of saline so that 0.1 ml contained 50 U. One application site or, in the case of larger muscles, two application sites were used for BTX-A infiltration.

Study design and statistical analysis

No interventions in the rehabilitation programmes were preformed – physio- and /or occupational therapy programmes remained the same before, during and after the study. All patients were assessed by the same neurologist, Parkinson's disease nurse and occupational therapist on six occasions at one-month intervals (Table 2). The patients' responses were recorded on new assessment sheets on each occasion without referring to previous results. At day one, the patients were clinically examined and assessed using AFT. At every subsequent visit, besides clinical examination and AFT, SAFI was also administered. Cross-over was done at visit 4 unless the patient still reported benefit of the therapy. If there was still a benefit of the botulinum toxin, the cross-over change was done after the benefit wore-off (Table 1). At the second visit after starting the treatment, some patients could opt for a top-up if there was no effect or the effect was mild and unsatisfactory. Only conditions with defined patterns and selected muscles were treated and fixed dosages were injected (Table 2). Injection points were defined by an electromyographic atlas.[15]

Table 1 Study design.

Visit	Day	Description
1	0	clinical examination, AFT, BTX/placebo, video recording
2	30 ± 3	clinical examination, AFT, SAFI, video recording
3	60 ± 6	clinical examination, AFT, SAFI, video recording
4	90 ± 9	clinical examination, AFT, SAFI, cross-over, BTX/placebo, video rec.
5	120 ± 12	clinical examination, AFT, SAFI, video recording
6	150 ± 15	clinical examination, AFT, SAFI, video recording

Table 2 Sites of application of Botulinum Toxin Type A and dosages used in the study.

Muscle	Dosage
Flexor digitorum superficials (FDS)	50 U
Flexor digitorum profundus (FDP)	50 U
Flexor carpi ulnaris (FCU)	75 U
Flexor carpi radialis (FCR)	75 U
Biceps brachii (BIC)	150 U
Brachioradialis (BR)	150 U
Pronator (PRO)	100 U
Extensor digitorum communis (EDC)	150 U
Opponens pollicis (OPP)	75 U

Despite the cross-over design, we analysed the data using simple nonparametric matched-pairs comparisons between placebo and BTX difference scores. We opted for this approach for the following reasons: because the study design minimised the possibility of carry-over effect, because we followed the authoritative advice not to test for carry-over,[16] because the groups were balanced so adjusting for period effect would have been meaningless,[16] and because the data were closer to ordinal then being of truly quantitative nature. For testing the scale difference scores, we used the exact Wilcoxon matched-pairs signed-rank test, while for dichotomised data (score improvement vs. no improvement) we used the exact McNemar test. Data analyses were performed using SPSS for Windows 15.0 software (SPSS Inc, Chicago, IL, 2007).

Results

The demographic and clinical characteristics of the patients are summarized in Table 1. The mean age of the patients was 31.1 years (SD 14.3 years). They all had long-term spasticity, on average for 10.8 years (SD 6.6 years). Two of the patients had spasticity because of cerebral palsy; the other patients had spasticity acquired later on in the life (one patient after bench meningoencephalitis, one patient after head trauma, one after neurosurgical extirpation of haemangioma, the rest of the patients had spasticity after CVI). Among those with acquired spasticity, four patients had left-sided hemiparesis and four had right-sided hemiparesis.

Table 3 Demographic and clinical data on the patients.

Patient	Age	Gender	Handedness	Diagnosis	Duration (years)*	Muscles treated
1	16	male	right	Right-sided spastic-dytonic hemiplegia; Dyskinesias	14	BIC, FCU, FCR
2	43	male	right	Right-sided spastic hemiplegia	20	BIC, BR, FDS, FDP
3	17	male	right	Cerebral palsy; Spastic-dystonic syndrome	17	BIC
4	15	female	right	Cerebral palsy; Spastic paresis	15	PRO, FCR, FCU
5	46	male	right	St. after CVI; Left-sided spastic hemiplegia	9	BIC, FDS, FDP
6	46	female	right	St. after CVI; Left-sided spastic hemiplegia	5	FCZ, FCR, OPP
7	31	female	right	St. after head trauma; Left-sided spastic hemiplegia	0	FDP; FDS; AP, BR; BIC
8	18	male	right	St. after bench meningoencephalitis; Right-sided spastic hemiplegia	3	FCU, FCR, FDP, FDS
9	51	male	right	St. after CVI; Right-sided spastic hemiplegia	3	EDC
10	28	female	right	St. after operation of haemangioma; Left-sided spastic hemiplegia	0	BIC, PRO, FCR, FCU, FDP, FDS

* Duartion of symptoms before therapy.

The AFT scores increased more after BTX therapy (by 0.4 on average, range 0-2) then after placebo (by 0.1 on average, range 0.1), but the difference was not statistically significant (P=0.500). On the other hand, the difference in SAFI scores in favour of BTX was statistically significant (mean improvement 2.8, range 0-5; vs. mean improvement 0.6, range 0.3 under placebo; P=0.016).

Neither of the scores worsened in any patient either after BTX treatment or after placebo. The tests on dichotomised data confirmed the results obtained with the original scores: 3 patients improved after BTX vs. 1 after placebo regarding AFT (P=0.500), and 8 patients improved after BTX vs. 2 after placebo regarding SAFI (P=0.031).

Discussion

The results of our study confirmed the beneficial effect of Botulinum Toxin Type A for treatment of spasticity and dystonia in upper limbs. However, the main aim of our study was to clarify functional benefit in the affected hand. As already pointed out by previous research,[17] the functional impact of this treatment needs further clarification. It has been suggested that any improvement in script is important while treating writer's cramp with BTX, but impossible to quantify objectively.[18] On the other hand, most of the patients' reports lack objective or quantifiable response variable.[19]

In our study, there was only one patient with improved score in AHF under placebo and three under the active substance. The patients themselves, however, reported a benefit after BTX application. This benefit was objectively observable when comparing the patients' performance of hand function subtests using video assessment. These changes only influenced the quality of performance on some subtests, but did not influence the final AHF score. The patients themselves were able to express perceptions of their own hand function using the 0-5 self-assessment scale. Eight out of the ten patients expressed BTX benefit in this way. Hence, the scale appears to be practical and helpful in describing how patients perceive their response to the treatment. The scale also indicated a placebo effect as two patients reported some benefit under placebo.

Since some data indicate brain reorganisation following therapy with BTX, in the future it would be interesting to investigate whether structural changes in the brain take place after long-term therapy with BTX.

Conclusion

While there was no statistically significant improvement on the Assessment of Hand Function scale for the botulinum session, a more reliable difference in favour of treatment was found on the 0-5 self-assessment scale. We believe that the AHF test is not sufficiently sensitive or at least not superior to simpler global scales. Hence, we confirmed that measurement of focal disability does not entirely clarify functional changes after treatment with Botulinum Toxin.

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Research Review Paper ■

Definitions of Terms in Telehealth

Drago Rudel, Malcolm Fisk, Robert Roze

Abstract. Executive Agency for Health and Consumers supported European-wide project Telehealth Services Code of Practice for Europe – TeleSCopE aims to develop a comprehensive Code of Practice for Telehealth Services. The first output from the Telescope was a report on definitions, terminology and shared understanding of terms relating to telehealth. It is summarised in this article. In parallel in Slovenia, a working group mandated by the Slovenian Medical Informatics Society Executive Board to prepare a draft document for a national telehealth strategy, has prepared the definitions of three basic terms: telemedicine, telehealth and telecare in the Slovenian language. They submitted the definitions to the Board for Standards in Healthcare at the Ministry of Health to include them into the growing Glossary of Terms in Healthcare. These definitions are also presented in this article.

Definicije pojmov na področju zdravja na daljavo

Izvleček. Članek predstavlja metodologijo in rezultate (definicije pojmov) evropskega projekta TeleSCopE, ki je namenjen vzpostavitvi standarda za področje storitev zdravja na daljavo (telehealth). Vzporedno s projektom potekajo aktivnosti tudi v Sloveniji. Upravni odbor Slovenskega društva za medicinsko informatiko je oblikoval delovno skupino, ki pripravlja Izhodišča za nacionalno strategijo zdravja na daljavo, ki vključuje tudi telemedicino. Ta delovna skupina je poenotila razumevanje in definicije pojmov telemedicina, zdravje na daljavo in oskrba na daljavo (telecare), ki so podane v tem prispevku. Predloge definicij, ki jih prav tako predstavljamo v članku, je posredovala Odboru za zdravstveno-informacijske standarde pri Ministrstvu za zdravje, da jih uvrstiti v (zdravstveni) Terminološki slovar.

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Background

There are clear indications that telehealth can help reduce costs and be as effective as or more effective than traditional forms of care. Much of the evidence, however, is fragmented and based on pilot applications. The context is one where telehealth is generally not embedded into mainstream service delivery.

However, there are hurdles to the adoption of telehealth technologies because of misunderstandings around its role or simply because users/patients and also healthcare professionals don't know about its potential. In different EU countries different terms may be used to describe the same services e.g. telemonitoring or telemetry. Their understanding is usually influenced by people's experience or their personal or professional view. Also definitions for those terms may differ because they see service provision from different perspectives. A clear perspective on terms used around telehealth is needed as definitions of terms related to telehealth have not yet been agreed, neither in Europe nor globally. Key terms were recognised as telehealth, telemedicine and telecare.

Executive Agency for Health and Consumers has partially supported a European wide project called *Telehealth Services Code of Practice for Europe – TeleSCopE*.[1] In the project, there are 11 partners from 7 EU MS: 4 user representatives, 2 academic, 7 SMEs and institutes. The primary objective of TeleSCoPE is to develop a comprehensive Code of Practice for Telehealth Services. The main outcome of TeleSCopE should be an adoption of the Code and its use within member states to underpin service frameworks that contribute to the well-being of EU citizens. The project directly supports EC Action Point to "improve confidence in and acceptance of telemedicine".[2] It is aiming at influencing European-wide confidence and acceptance of telehealth by influencing a common approach on the political level (harmonisation), on the semantic level (agreeing common priorities), and on the level of education and awareness raising (evaluation, monitoring and analysis and reflection on good practice). TeleSCoPE will, through establishing service standards, help establish relationships of trust between patients and providers and contribute to overall health and well-being. The standards will provide a quality benchmark for service regulation in member states.

One of the Workpackages of the TeleSCoPE project deals with definitions, terminology, shared understanding and literature review. The first output from the project was a report on definitions, terminology and shared understanding of terms relating to telehealth which are summarized in this article. This document presents a glossary of terms. It is the outcome of an intensive literature overview that brought together existing definitions related to telehealth, subjected them, where necessary, to critical assessment, and amended where appropriate to fit with the understanding of project partners. The glossary reflects, therefore, a particular understanding of telehealth, its scope, services and technology.

Methodology

One of the aims of the literature review within the TeleSCoPE was to collect and critically analyse the existing definitions for telehealth and related terminology, service models, services, domains covered by services, and fields of applications.

Reference Documents Resources

Different resources were used when identifying definitions. The main sources of existing definitions were documents of professional bodies dealing with telemedicine and/or telehealth. European and wider international sources, as follows, have been drawn upon:

- COCIR – European Coordination Committee of the Radiological, Electro-medical and Healthcare IT Industry[3]

- ATA – American Telemedicine Association[4]
- NIFTE – National Initiative for Telehealth, Canada[5]
- IiE – EC EAEAC project – ImPaCT in Europe – Improving Person Centred Technology in Europe[6]
- PERSA – Association of Social Support Monitoring Services[7]
- ISfTEH – International Society for Telemedicine and eHealth[8] (represented in the TeleSCoPE consortium through Lievens Lanckman)
- Telecare Services Association, UK[9] (A member of the TeleSCoPE consortium)

Additional resources used included relevant strategic and policy documents, the most notable relating to which is the communication from the European Commission on telemedicine.[8] Several articles in professional journals and the outputs from relevant European projects were also reviewed as a potential resource of definitions. Reports from European projects (within FP6, FP7 and AAL programmes) and the proceedings of some international conferences/workshops were also used. Internet resources such as *Wikipedia*, *Telecare Aware* and *WhatIs* were also used, on occasion, to obtain pointers. The TeleSCoPE project partners also contributed their own definitions for some most critical terms.

The source of each definition is indicated in the glossary. Where definitions closely relate to a primary source but have been amended, these are indicated by an asterisk [*]. Those definitions that have been developed by TeleSCoPE partners are marked "TeleSCoPE".

Specialised technical terms used in telehealth systems that have already been well defined by standardisation organisations (e.g., ISO TC 215, CEN TC 251 and others) are not a part of the glossary. Paid resources like *Mondeca Health Care terminology for eHealth* have not been used.

Database on Information Resources and the TeleSCoPE Reference Literature Library

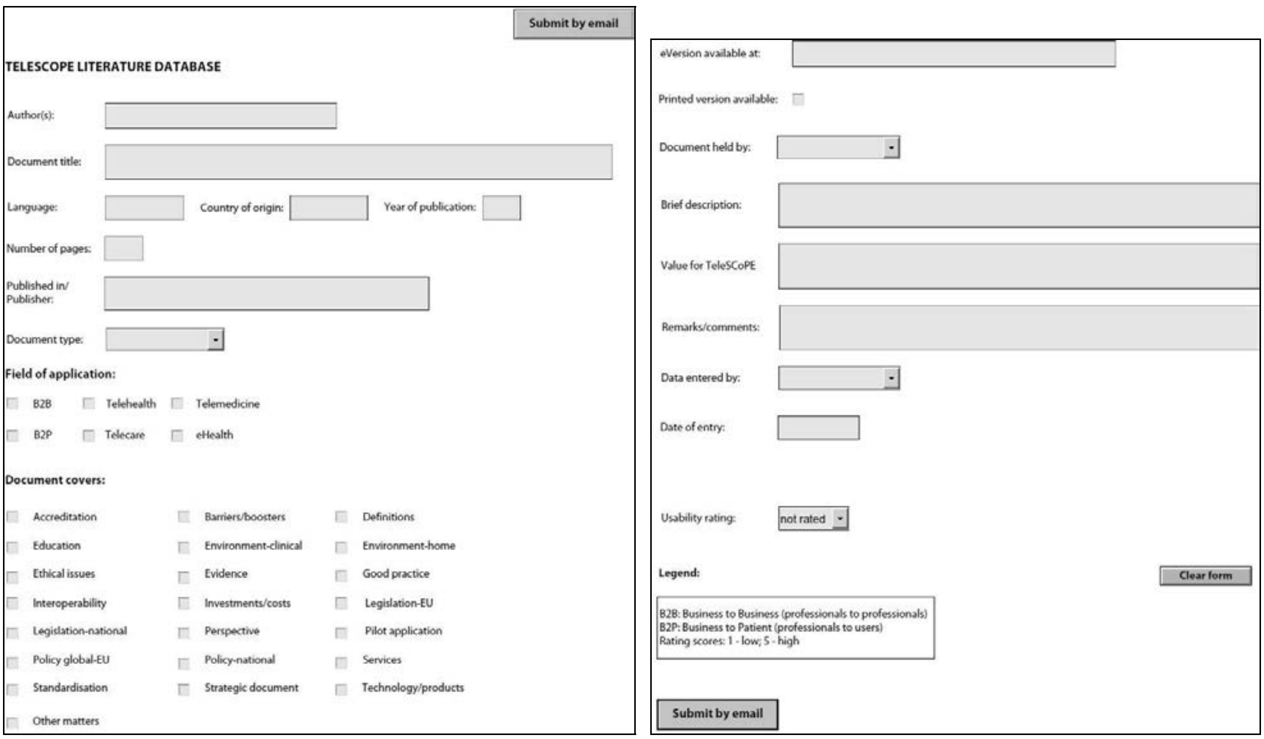
An Excel spreadsheet was created to serve as a reference literature database of information resources. Its structure is given in Table 1.

Table 1 Structure of the Literature Database.

No	Field	No	Field	No	Field
1	No	18	Education	35	Legislation-EU
2	Ref_No	19	Ethical_issues	36	Pilot_application
3	Author(s)	20	Interoperability	37	Services
4	Document_title	21	Legislation-national	38	Technology_product
5	Language	22	Policy-global-EU	39	eVersion_available_at
6	Number_of_pages	23	Standardisation	40	Printed_version_available
7	Country_of_origin	24	Other_matters	41	Document_held_by
8	Year_of_publication	25	Barriers_boosters	42	Data_entered_by
9	Published_in_publisher	26	Definitions	43	Brief_description
10	Document_type	27	Environment-Clinical	44	Value_for_TELESOPE
11	B2B	28	Evidence	45	Remarks_Comments
12	B2P	29	Investments_Costs	46	Date_of_entry
13	Telehealth	30	Perspective	47	Usability_rating
14	Telecare	31	Policy-National	48	Auto_Reference_Vancouver
15	Telemedicine	32	Strategic_document	49	Reference_Vancouver
16	eHealth	33	Environment-Home		
17	Accreditation	34	Good_practice		

References, and in some cases, links to relevant documents, were collected by the project partners. For this purpose a dedicated PDF template was developed by two of the project members (MKS, ITC-CNR). Each filled template was sent as an XML file by email to the responsible partner (MKS) for further processing. The XML formatted files were then imported into the XLS database. In some cases references were provided as plain text only and data were inserted into the spreadsheet manually. The collection template is presented in Figure 1.

In addition to the reference database, the *TeleSCoPE Reference Literature Library* was created containing documents in electronic and printed form. The library is held by the responsible partner (MKS).



Submit by email

TELESCOPE LITERATURE DATABASE

Author(s):

Document title:

Language: Country of origin: Year of publication:

Number of pages:

Published in/ Publisher:

Document type:

Field of application:

B2B Telehealth Telemedicine

B2P Telecare eHealth

Document covers:

Accreditation Barriers/boosters Definitions

Education Environment-clinical Environment-home

Ethical issues Evidence Good practice

Interoperability Investments/costs Legislation-EU

Legislation-national Perspective Pilot application

Policy global-EU Policy-national Services

Standardisation Strategic document Technology/products

Other matters

eVersion available at:

Printed version available:

Document held by:

Brief description:

Value for TeleSCoPE

Remarks/comments:

Data entered by:

Date of entry:

Usability rating: not rated

Legend: Clear form

B2B: Business to Business (professionals to professionals)
B2P: Business to Patient (professionals to users)
Rating scores: 1 - low; 5 - high

Submit by email

Figure 1 Template for collection of data for literature review.

Literature Classification

The collected reference documents were classified using the following primary groups of classifiers:

- Type of document (paper, book, article, communication);
- Scope of document (telehealth, telecare, telemedicine, eHealth);
- Field of application covered (definitions; strategy; policy – EU, global, national; education; ethical issues; legislation – EU, national; standardisation; interoperability; accreditation; technology/product description; etc.);
- Type of activity (pilot application, good practice; services; evidence; investments/costs assessment; etc.);
- Locus of the activity (home environment; clinical environment, regional; international);
- Barriers/boosters (obstacles/enablers) for telehealth services.

The collected definitions in the glossary were critically assessed by TeleSCoPE project partners in the context of a broad view of existing and potentially new telehealth services. This broad view covers not only the domain of medicine but also of personal well-being. It follows from this that partners adjusted some of the most important definitions in a way that helped to move the focus from illness to a broader frame of reference that embraces both health and lifestyle issues. Such a move reflects a paradigm shift that affirms the view of partners about the primary importance of telehealth, rather than telemedicine, in the pursuit of key European policy objectives.

What is Telehealth?

TeleSCoPE partners understand telehealth as

the means by which technologies and related services at a distance are accessed by or provided for people and/or their carers at home or in the wider community, in order to facilitate their empowerment, assessment or the provision of care and/or support in relation to needs associated with their health (including clinical health) and well-being. Telehealth always involves and includes the service user or client. It includes remote patient management.

The foregoing definition largely accords with that of COCIR.[10] But the TeleSCoPE definition affords telehealth with a broader frame of reference that extends beyond long-term conditions and places greater emphasis on the use by and empowerment of patients/users. The TeleSCoPE definition (above) seeks, therefore, to ensure that telehealth responds to congenital disability, frailty, preventative and public health agendas as well as issues relating to lifestyles and assessments or treatment responding to illness or chronic conditions.

COCIR assert that the term telehealth covers systems and services linking patients with care providers to assist in diagnosing, monitoring, management and empowerment of patients with long-term conditions (chronic patients). They add that telehealth solutions use devices (interactive audio, visual and data communication) to remotely collect and send data to a monitoring station for interpretation and to support therapy management programs and to improve patients' knowledge and behaviour.

The range of devices, indicated by COCIR as supporting telehealth solutions, are rightly noted as embracing systems and components (patient interfaces in hardware and software; sensors/peripherals; operating software and applications intended for care provider usage; clinical content and intelligence; data transmission, storage and intelligent routing). These, they recognised, are associated with services that address healthcare delivery, diagnosis, consultation and treatment as well as education/behavioural modifications and transfer of medical data.

Scope of Telehealth

A definition that helps in understanding how telehealth fits with other terms and service areas was necessary in order to enable the scope and boundaries of telehealth services to be made. This, in turn, facilitated a better understanding of the requirements for and the limitations of the technologies being used within telehealth services. All TeleSCoPE project partners were invited to contribute their views on such matters by which a shared understanding was subsequently reached.

Key interrelated terms were identified including telehealth, telemedicine, telecare, social alarms, eHealth and assistive technologies. The partners agreed on an initial understanding of the scope and the relationships between these terms. The result is presented in Figure 2. Encompassing them all is recognition that all contribute to personal well-being – hence personal wellbeing offering the broadest, and arguably indisputable, domain.

There are two major sub-domains within that domain: assistive technologies aiming at supporting disabled and frail people, and eHealth covering needs of patients. The telecare domain falls almost completely into the eHealth domain – involving social alarms and telehealth. An element of social alarms is indicated as falling outside of eHealth in recognition of those applications that relate to e.g. personal security and property management. Telemedicine, being concerned more narrowly with the more clinical aspects of health and well-being (and including services within which clinicians exchange data and information) becomes a sub-domain of telehealth.

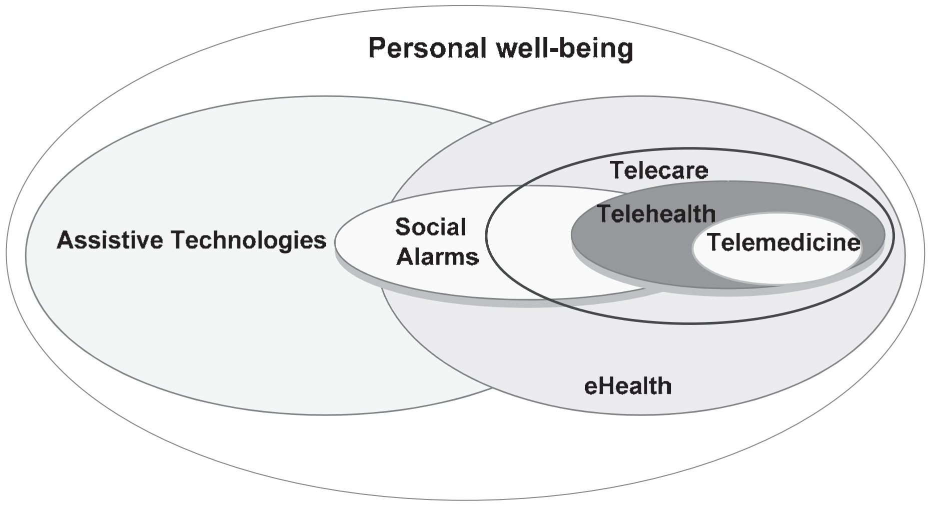


Figure 2 Scope of Telehealth by TeleSCoPE.

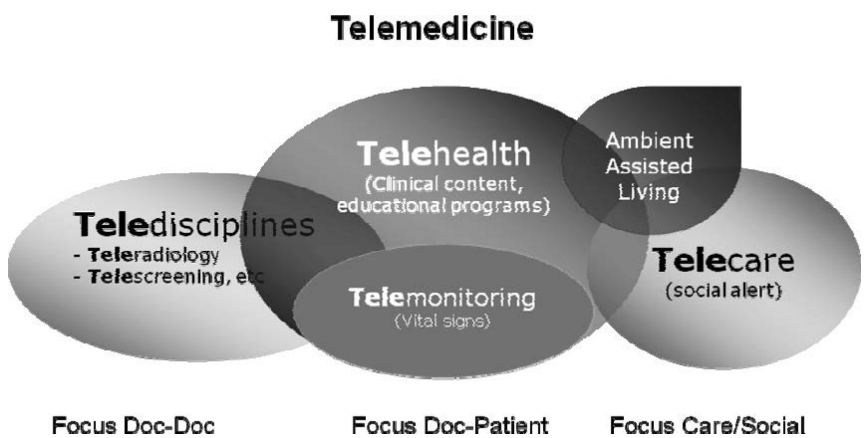


Figure 3 Scope of Telemedicine by COCIR.[9]

Having set out the scope of telehealth in this way it must be recognised that the boundaries and overlaps are not set in stone. Some adjustment, though not perhaps radical change, is envisaged as our understandings of telehealth applications develop.

The TeleSCoPE understanding of the telecare domains as depicted in Figure 2 is in line with that suggested by Telecare Aware[11] as one where "there is an emerging case to use the term 'telecare' also as an overarching term for all types of care, including health care, delivered at a distance".

The domain model for telemedicine/telehealth offered by COCIR[9] is, in some respects, different from that of the TeleSCoPE partners (see Figure 3). For COCIR, the overarching telemedicine domain includes telehealth, ambient assisted living, telecare, telemonitoring and several teledisciplines. Accordingly, telemedicine in the view of COCIR "includes all areas where medical or social data is being sent/exchanged between at least two remote locations, including both Caregiver-Patient/Citizen as well as Doc-to-Doc communication".[10]

The foregoing discussion has made it clear that the TeleSCoPE context needs to be understood as one which recognises telehealth as supporting both health and well-being. In other words it is recognised that health cannot be seen purely in clinical terms. Rather it is concerned with people's lives and people's homes – where services using telehealth technologies are provided by agencies; or, importantly, technologies are harnessed by individuals. Therefore, from the TeleSCoPE point of view, the COCIR domain framework has shortcomings. It is argued that as medical services are only a part of healthcare services, telemedicine should be a sub-domain of telehealth and not vice versa.

To further support the TeleSCoPE view, Table 2 presents what can be seen as some main differences in focus between telemedicine and telehealth.[12] In essence, this table points to telemedicine as relating to a service paradigm that reflects a "medical" rather than "social" model of care and support. In practice there is substantial overlap, but a TeleSCoPE promotes a move from the former towards the latter.

Table 2 Understanding of Telemedicine vs. Telehealth.

Telemedicine	Telehealth
Technologies for illness	Technologies for wellness (well-being)
Clinician and nurse led	Service or user led
Institutional context	Home or community context
Focus on patients	Focus on people
Control and monitoring of patient	Self-management by user
"Treatment" may promote dependency	"Empowerment" can support independence

WHO makes a distinction between telemedicine and telehealth through which it also defines also their domains. They affirm that "telehealth is understood to mean the integration of ICT systems into the practice of protecting and promoting health, while telemedicine is the incorporation of these systems into curative medicine…".[13] We may derive from this that, for WHO, telemedicine is a sub-domain of telehealth.

Definitions of Terms

Terms that relate to healthcare services, solutions and systems were collected from the range of literature noted below. A Glossary of Terms in Telehealth has been complied (Table 3).

From the TeleSCoPE point of view a clear perspective on the terms used around telehealth has been needed in view of the fact that terms related to telehealth have, as yet, neither been agreed in Europe nor globally. In EU countries different terms may be used to describe the same service e.g. telemonitoring or telemetry. Their understandings are usually influenced by people's experience or their point of view (as professionals, users, patients). For healthcare workers, "telecare" could mean a social service at a distance while for others it could be a healthcare service delivered for e.g. people with long-term conditions. There are also several other factors that have influencing people's understandings. For example, the telemedicine/telehealth industry (represented by COCIR[9]) understands and defines terms differently from politicians.[2]

Table 3 Glossary of Terms in Telehealth.

Term	Definition	Source
Ablement	see Reablement	
Accessibility	Physical and sensory access to buildings, services and information. Relates to matters such as physical design, lighting, colour, textures, technologies, visual and audible cues.	TeleSCoPE
Accreditation	A process by which acknowledgement can be obtained for services that are accessible, appropriate and delivered according to agreed quality standards.	TeleSCoPE
Activity monitoring	The monitoring of activity (movement or interaction with the environment) in order to identify situations or circumstances that reflect adverse changes in or threats to personal well-being. Lifestyle Monitoring represents an extension of Activity Monitoring.	TeleSCoPE
Ageing	The process by which minor impairment multiply (e.g. in relation to sight, hearing, dexterity, mobility and cognition), potentially leading to disability and dependency.	IiE [*]
Ambient Assisted Living (AAL)	Independent living supported by unobtrusive systems, services and devices within the home.	TeleSCoPE
Ambient Intelligence (AI)	The intelligence, derived from systems and devices in built into environments that support Ambient Assisted Living (AAL).	TeleSCoPE
App	An abbreviation for 'application'. Software for use in devices such as mobile phones, TVs or tablet PCs (including that which can relate to personal health and well-being).	TeleSCoPE
Assistive Technology	Any item, piece of equipment, or product system that is used to increase, maintain, or improve the functional capabilities of individuals with disabilities. See also Electronic Assistive Technology	IiE
Augmentative and Alternative Communication (AAC)	Any means of communication that supplements handwriting or speech where either of the latter are impaired.	IiE [*]
Barrier-Free Design	See Design for All	
Bluetooth	An industrial specification for wireless personal area networks (PANs) that connect and exchange information between devices (including mobile phones, laptops and PCs) over a secure, globally unlicensed shortrange radio frequency.	ATA [*]
Broadband	Communications (e.g., broadcast television, microwave, and satellite) capable of carrying information, images and data via a wide range of frequencies over a segment of the total bandwidth available.	ATA [*]
Call Centre	Call centres receive and respond to incoming telephone calls. They may also handle letters, faxes and e-mails. See Monitoring Centre.	TeleSCoPE
Carephone	see Social Alarm	
Certificate	electronic 'key' that a secure server checks for before allowing a user access	MIT
Certification	see Accreditation.	
Clinical Information	Information relating exclusively to patient care rather than administrative matters.	ATA [*]
Community Alarms	see Social Alarms	
Competency	The specific knowledge, skills, judgement and personal attributes required to practice safely and ethically in a designated role and setting	NIFTE [*]
Computer-Based Patient Record (CPR)	An electronic form of individual patient information.	ATA [*]
Confidentiality	The fundamental requirement whereby personal information is safeguarded and accessible only in agreed circumstances (where appropriate, to authorised	TeleSCoPE

Term	Definition	Source
	persons) and/or in relation to the fulfilment of service objectives that are normally agreed with the user / patient.	
Conformance	Conformance to standards refers to the ability of a product or system to perform a set of functions according to specifications that are defined within a standard.	NIFTE [*]
Consent	see Informed Consent	
Consulting Site	see Service Provider Site	
Control Centre	see Monitoring Centre	
Data Security	The protection of personal data from unauthorized or unintentional loss, theft, access, use, modification, or disclosure.	NIFTE [*]
Design for All	Facilitates access to environments, products and services for the largest range of people (i.e. including people with physical or sensory impairments). Is an equivalent term to Universal Design.	IiE [*]
Diagnostic equipment	Devices that can provide medical data to assist diagnosis. When linked to a computer can be considered as Peripheral Devices.	ATA [*]
Digital Imaging and Communication in Medicine (DICOM)	A standard for the identification, formatting and communication of medical images	ATA [*]
Disability	Disability is a complex phenomenon, reflecting an interaction between features of a person's body and environment, whereby full and effective participation in economic and social life may be hindered.	TeleSCoPE
Disease Management	A continuous coordinated health care process that seeks to manage and improve population's health	TeleSCoPE
Domotics	see Home Automation	
Duty of care	The legal duty of a health or social care professional to a person who is receiving care and support in respect of an identified need.	TeleSCoPE
e-Health	eHealth describes the application of information and communication technologies across the whole range of functions that affect the health sector. It aims to improve significantly the quality, access and efficacy of healthcare for all.	EC CT i2010
eInclusion	The policy direction of the European Commission that affirms the priority given to the social inclusion of citizens in ways furthered through the appropriate use of methods of electronic communication	TeleSCoPE
Electronic Assistive Technology	Assistive Technology which communicates electronically with other devices and/or the user / patient. See Assistive Technology.	IiE [*]
Electronic Health Record (EHR)	An electronic record that can be maintained directly by users / patients that securely holds information and data relating to their health history, medication and care received. Includes Personal Health Records.	TeleSCoPE
Electronic Patient Record (EPR)	An electronic record regarding information and data of users / patients by which clinical decisions regarding their treatment can be made.	TeleSCoPE
Emergency Response System	see Social Alarm	
Empowerment	A process through which people gain or are afforded greater control over decisions and actions affecting their lives.	TeleSCoPE
Environmental control device	A piece of equipment that helps people with a physical or sensory impairment to control their environment and help them to undertake day to day tasks safely.	TeleSCoPE
Good Practice	Practice that is informed, shared with others and accords operates according to sets of principles that help fulfil aims and objectives associated with appropriate political, economic and social goals.	TeleSCoPE
Governance	The function of determining an organisation's direction, objectives, policy and practice frameworks in order to effect effective service delivery.	TeleSCoPE
Health Care	Any individual who, directly or indirectly, provides health care at the hands-on	Kluge[15]

Term	Definition	Source
Professional (HCP)	level in a professional capacity.	
Health Coaching	see Health Training	
Health Record	see Electronic Health Record	
Health Training	The use of techniques based on psychological evidence to help people change behaviours that are known to cause ill-health. Also known as Health or Motivational Coaching.	TeleSCoPE
Home Automation	A field of building automation by which affords users greater control over their home environment and can enhance usability, security and comfort. Also known as Domotics.	IiE [*]
Home Telehealth	see Telehealth	
Hub Site	see Service Provider Site	
Impairment	Reduced capacity arising out of congenital or acquired physical or sensory impairments, health conditions, ageing and frailty. Impairments can lead to disability through factors relating to the design of environments, products, systems and services.	IiE [*]
Independence	The circumstances by which individuals remain, with or without care and support, in control of aspects of their lives that are most important to them.	TeleSCoPE
Independent Living Services	Services designed to enhance the abilities of individuals to live independently and, if appropriate, to secure and maintain employment.	IiE
Information and Communication Technology (ICT)	An umbrella term that includes communication devices or applications including radio, television, mobile (cell) phones, computer hardware, software and their networks, satellite systems, etc. As well as the services and applications associated with them – such as video-conferencing and distance learning.	IiE [*]
Informed Consent	Voluntary permission given, in a context of understanding by the user / patient (or where appropriate their carers), to the purpose, procedures, benefits, risks and rights relating to their use of a technology or service.	TeleSCoPE
Intelligent Home	see Smart Home	
Interface	see User Interface	
Interoperability	Interoperability refers to the ability of two of more devices or systems to interact with one another and exchange information in order to achieve predictable results.	NIFTE
Lifestyle Monitoring	The monitoring of environmental conditions, activity (movement or interaction with the environment) and physiology in order to identify situations or circumstances that reflect adverse changes in or threats to personal well-being. Represents an extension of Activity Monitoring.	TeleSCoPE
Medical model of disability	The model of disability and ageing implies that people are disabled as a consequence of their own condition, and seeks to either remedy the impairment through medication, rehabilitation and surgery, or through adaptive aids and equipment.	IiE
Medical / Nursing Call Centre	A call centre that answers incoming telephone calls from patients and may also respond to letters, faxes, e-mails and similar written correspondence. May provide basic health information and guidance to users / patients and act as an initial triage point for patients. See Monitoring Centre.	ATA [*]
Medication compliance	A term used to signify patient accordance with treatments and therapies decided upon by the doctor or other health professionals.	TeleSCoPE
Medication concordance	A term used to signify patient accordance with treatments and therapies decided upon between the patient and the doctor or other health professionals.	TeleSCoPE
mHealth	Mobile communications and network technologies for healthcare.	Robert Istepanian
Mobile Telehealth	The provision of health care services with the assistance of a mobile unit that can	ATA [*]

Term	Definition	Source
	be located at a distance from normal medical facilities.	
Monitoring Centre	A monitoring centre includes call centre functions but carries additional responsibility for people, buildings, equipment, vehicles, etc. that can relate to the operation of services concerned for personal health and wellbeing. See Call Centre.	TeleSCoPE
Motivational Coaching	see Health Training	
Nursing Telepractice	see Telehealth Nursing	
Originating Site	see Patient / User Site	
Patient / User Encounters	A patient / user encounter occurs where there is real time personal communication with a service provider (who may be a health practitioner) on the basis of which decisions may be agreed regarding care, support and treatment.	ATA [*]
Patient / User Site	The place where the patient / user is located during a telehealth encounter or remote consultation (CMS). Also known as Spoke or Originating Site. Complements the Service Provider Site.	ATA [*]
Peripheral Device	Devices that communicate with a computer, carephone or other device, e.g. scanners, mouse pointers, printers, keyboards; pulse oximeters, weight scales, fall detectors, etc. Includes some Diagnostic Equipment.	ATA [*]
Person Centred Technology (PCT)	Person Centred Technology (PCT) is technology specifically designed around the needs of the individual and, where appropriate, their carers. It includes Electronic Assistive Technologies.	IiE
Personal (Emergency) Response Systems (PERS)	see Social Alarm	
Personal Health Record	see Electronic Health Record	
Personalisation	The design and development of services in ways that respond to the expressed wishes and needs of the people who see k access to them.	IiE [*]
Picture Archiving and Communications Systems (PACS)	PACs provide centralised storage and access to medical images over information systems.	ATA
POTS	Acronym for Plain Old Telephone Service.	ATA
Presenter (Patient Presenter)	A person, trained where appropriate in the use of the equipment, to assist in a patient / user encounter at the patient / user site and, to perform any hands-on activities to assist in any remote examination.	ATA [*]
Privacy	The state afforded to users / patients whereby their right to control information (including images and data) relating to their health and lifestyles is both recognised and respected.	TeleSCoPE
Qualified Staff	Those staff having the credentials and competence to perform specific acts as a result of their training and/or experience – potentially recognised through registration, certification, licensure.	NIFTE [*]
Quality Assurance	The process by which services or aspects of services, following some form of assessment or accreditation, are deemed to meet appropriate levels of quality.	NIFTE [*]
Reablement	An approach or a philosophy within care at home services which aims to help people "do things for themselves", rather than "having things done for them".	TeleSCoPE
Real Time	see synchronous	
Referral Site	see Service Provider Site	
Rehabilitation	The process of restoration of skills by a person who has had an illness or injury so as to regain maximum self-sufficiency and function in a normal or as near normal manner as possible.	Medicine.net

Term	Definition	Source
Remote Monitoring	The use of devices that collect patient / user vital sign and other data and effect its transmission, in real-time or periodically, to a monitoring centre.	AdvaMed[16] [*]
Remote Patient Management (RPM)	Remote evaluation and non-operative treatment of a user / patient, using communications technology.	TeleSCoPE
Risk Management	The process by which risks are managed or mitigated in order to reduce the chance or possibility of danger, loss or injury.	NIFTE [*]
Safe walking	see Wandering	TeleSCoPE
Safeguarding	The processes and procedures, normally involving several agencies of service provision, whereby vulnerable adults and children are protected against different forms of abuse (or power).	TeleSCoPE
Safety Alarm	see Social Alarm	TeleSCoPE
Security	see Data Security	
Self Monitoring	The periodic use of a device by the patient/user to obtain measures relating to his/her health and wellbeing.	TeleSCoPE
Sensor	Any device that receives a signal or stimulus and responds to it in a distinctive manner.	TeleSCoPE
Service Provider Site	The place, at a distance, where the service provider is located and receives information and/or communicates with the user/patient. Otherwise known as the Hub, Referral or Consulting Site.	ATA [*]
Smart Home	A home with installed technologies the use, or automatic operation, of which can assist the resident to live with e.g. greater comfort or safety. Also known as Intelligent Home.	TeleSCoPE
Social Alarm	A device located in the home which, when activated, communicates with a responder and can send of information relevant to the user's well-being. Otherwise known as a carephone, community alarm, safety alarm or (personal) emergency response system (PERS).	TeleSCoPE
Social exclusion	see Social Inclusion	
Social inclusion	The state whereby people are engaged with the social, economic and political activities commensurate with citizenship and normal living. The converse of social exclusion.	IiE [*]
Social model of disability	In contrast to the medical model, the social model sees people as disabled or enabled by the social context in which they function.	IiE
Spoke Site	see Patient / User Site	
Standards	Documented agreements containing technical specifications or other precise criteria to be used consistently as rules, guidelines or definitions of characteristics to ensure that materials, products, processes and services are fit for the purpose.	ISO
Store and Forward (S&F)	A type of telehealth encounter or consultation where digital images of a patient/user are forwarded asynchronously in order to assist in diagnosis or treatment.	ATA [*]
Synchronous	Simultaneous (e.g. with regard to transmission of data, speech and information). Also known as Real Time.	TeleSCoPE
Tele-assistance	The assistance given when a health professional or other person, at the location of the user/patient (the originating site), assists the carrying out of a medical act guided by a doctor or other health professional at the service provider site.	TeleSCoPE
Telecare	The means by which technologies and related services at a distance are accessed by or provided for people and/or their carers at home or in the wider community, in order to facilitate empowerment or the provision of care and/or support in relation to needs associated with their health and well-being.	TeleSCoPE
Teleconferencing	Interactive electronic communication between multiple users at two or more sites which facilitates real time voice, video, and/or data transmission.	ATA [*]

Term	Definition	Source
Teleconsultation	The means by which clinicians and other healthcare practitioners use telephone or video-telephony to consult with users/patients and/or their carers.	COCIR [*]
Teledisciplines	The various disciplines (e.g. teleradiology, teledermatology, telepsychiatry, etc.) performed at a distance between a doctor and a patient/user, or between two healthcare professionals; through the use of ICT.	COCIR [*]
Telehealth	The means by which technologies and related services at a distance are accessed by or provided for people and/or their carers at home or in the wider community, in order to facilitate their empowerment, assessment or the provision of care and/or support in relation to needs associated with their health (including clinical health) and well-being.	TeleSCoPE
Telehealth Nursing	Telehealth nursing is the practice of nursing over distance using telecommunications technology.	NCSBN
Tele-Intervention	Tele-intervention is a therapeutic medical act which is performed remotely by a physician on a patient, without or with the local presence of other healthcare professional (e.g. telesurgery).	COCIR
Telematics	The use of information processing based on a computer in telecommunications, and the use of telecommunications to permit computers to transfer programmes and data to one another.	ATA [*]
Telemedicine	The delivery of medical care at a distance by clinicians and other health care staff, via telecommunications technologies. Telemedicine will sometimes involve and include the service user / patient.	TeleSCoPE
Telementoring	The use of audio, video, and other telecommunications technologies to provide guidance or direction.	ATA [*]
Telemonitoring	The use of communications technologies to remotely collect/send data relevant to the health and well-being of a user / patient to a monitoring centre to assist in diagnosis and monitoring.	COCIR [*]
Telepresence	The use of robotic and other instruments that enable a clinician to perform a procedure at a remote location by which he/she receives feedback or sensory information that contributes to his/her sense of presence.	ATA [*]
Telesurgery	Surgical procedures carried out remotely with the assistance of robotic devices and a real-time video and audio connection.	TeleSCoPE
uHealth	The notion by which services such as those under the rubric of telehealth offer ubiquitous (u) access.	TeleSCoPE
Universal design	see Design for All	TeleSCoPE
User Interface	The area in which users / patients interact with and, where appropriate, exercise control over devices.	TeleSCoPE
Videoconferencing	Real-time two way transmission of digitised video images between two or more locations.	ATA [*]
Videoconferencing Systems	Equipment and software to provide real-time two way transmission of digitised video images between two or more locations.	ATA [*]
Vital Signs	Health or activity measures that relate to a person's well-being. Included are such measures as relate to weight, blood pressure, blood oxygen level, body temperature, lung function and body movement.	TeleSCoPE
Wandering	An aspect of the behaviour of some people with dementia that can appear to (others to) lack purpose and may expose the patient / user to additional risk. An alternative term, not favoured, is Safe Walking.	TeleSCoPE
Well-being	Quality of life characterised by satisfactory levels of health and welfare.	TeleSCoPE

Note that where sources are indicated with an asterisk [*], the definition in question has been amended from that offered by the body in question.

Critical Analysis of the Definitions of Terms

Key terms associated with TeleSCoPE project are recognised to be "telehealth", "telemedicine" and "telecare". These are, of course, defined in the glossary along with definitions relating to service and technological contexts e.g. facets of care and support services, key devices, communications networks, databases, interoperability, etc.

For some terms several different definitions were found in the literature. These have, in some cases, been set aside (as inadequate or inappropriate for the TeleSCoPE context) but in many cases adopted or amended. It can be noted that different definitions were found for the key terms with which TeleSCoPE is concerned. These are discussed below.

European Commission Definitions

The European Commission, in its communication on telemedicine document,[2] defines telemedicine as "the provision of healthcare services, through the use of ICT, in situations where the health professional and the patient (or two health professionals) are not in the same location …". It does not define "telehealth" explicitly.

In the Staff Working Paper,[14] also addressing "telemedicine", the European Commission reaffirms the same understanding, with telemedicine embracing services which we might recognise as "telehealth" or "telecare".

COCIR Definitions

The European Coordination Committee of the Radiological, Electro-medical and Healthcare IT Industry (COCIR) has done substantial work to define terms relating to telemedicine and telehealth. Regarding the term "telemedicine", COCIR adopts the EU Commission definition[2] adding that "telemedicine is the overarching definition spanning telehealth, telecare and teledisciplines".[10] COCIR also opines that telehealth covers systems and services linking patients with care providers to assist in diagnosing, monitoring, management and empowerment of patients with long-term conditions (chronic patients)". It is suggested, however, that, in general, the COCIR definitions are closer to the needs of industry than those of the EC.

The TeleSCoPE project partners consider, furthermore, that the COCIR definition, in focusing on long-term conditions, can exclude technologies and services that relate to preventative and other agendas (e.g. concerned with lifestyles, frailty, falls). Consequently, TeleSCoPE partners have set definitions that move the focus from illness to a broader view of well-being.

ATA Definitions

The American Telemedicine Association (ATA) has done intensive work in this field, defining a variety of clinical terms and disciplines. The ATA closely associates telehealth with telemedicine, stating that telecare is "often used to encompass a broader definition of remote health care that does not always involve clinical services…".[4]

NIFTE Definitions

NIFTE wrote its strategic guideline document on telehealth in 2003[5] in which only one term – t "telehealth" – was used for all telecare and telemedicine services. The term "telemedicine" was used only in a historical context when referring to the documents in the past, e.g. "the earliest identifiable telemedicine activities in Canada …". This document contains also a chapter on definitions, where the term "telemedicine" was simply omitted.

IiE Definitions

The IiE project[6] adopted the definition of telehealth from WHO, hence telehealth is regarded as "the remote exchange of physiological data between a patient at home and medical staff at hospital to assist in diagnosis and monitoring (this could include support for people with lung function problems, diabetes etc). It includes (amongst other things) a home unit to measure and monitor temperature, blood pressure and other vital signs for clinical review at a remote location (for example, a hospital site) using phone lines or wireless technology". Telemedicine for IiE is, therefore, "the use of telecommunication to provide diagnostic and therapeutic medical information between patient and doctor over a distance, without necessitating they meet in person".

WHO Definitions

According to Darkins and Cary,[13] the World Health Organisation (WHO) makes a distinction between telemedicine and telehealth. They point to telehealth as meaning "the integration of ICT systems into the practice of protecting and promoting health, while telemedicine is the incorporation of these systems into curative medicine…". They observe that "telehealth corresponds more closely to the international activities of WHO in the field of public health. It covers education for health, public and community health, health system development and epidemiology, whereas telemedicine is oriented more towards the clinical aspects. The WHO definition of telemedicine is also adopted by Telecare Aware (see below).

Telecare Aware Definitions

Telecare Aware[11] posit a definition of telecare as "the continuous, automatic and remote monitoring of real time emergencies and lifestyle changes over time in order to manage the risks associated with independent living". This definition firmly associates telecare with "social" or "lifestyle" issues. It recognises, however, that there is an emerging case for using the term "telecare" as an overarching term for all types of care, including health care, delivered at a distance with communications technologies. Usefully they opine that "telecare and telehealth technologies will merge, and although the clients and patients they benefit are often one and the same individuals, it is still useful – at this stage of technological and linguistic evolution – to maintain a difference between the terms "telecare" and "telehealth".

For telemedicine, the WHO definition is adopted, viz. "Telemedicine is the practice of medical care using interactive audio visual and data communications.This includes the delivery of medical care, diagnosis, consultation and treatment, as well as health education and the transfer of medical data". Telemedicine, according to this definition, is therefore essentially doctor-to-doctor, with the patient somewhere in the system, and will typically involve consultation with specialists at a distance.

TeleSCoPE Definitions

The collected definitions in the glossary were critically assessed by the TeleSCoPE project partners in the context of their varied and broad view of existing and potentially new telehealth services. This view covered not only the domain of medicine but of wider personal well-being. This reflected what has been signalled as a paradigm shift towards a social model of care and support, by which we have a clearer understanding of telemedicine versus telehealth.

Because telehealth is a newly emerging concept, it is unsurprising that there should be some differences in the way that it is understood and key terms are used. In setting out these definitions, therefore, there is no criticism intended of definitions that have been set out elsewhere. As with any new term the core activities that are embraced and the boundaries that separate those activities from others must initially be explored and tested. TeleSCoPE furthers this process. We have noted, therefore, and have attempted to make sense of the way in which the interplay of key terms relating to telehealth, (most notably telemedicine and telecare) have often been used to embrace that area of services and technologies that we consider are most appropriately embraced by the term telehealth.

In essence, definitions provided in other contexts have been accepted, refined or added to. Where there is significant deviation from the definitions from such sources, this is noted. The foregoing discussion indicates where the justification for such deviations lie.

Separate attention was not given to most separate "tele" disciplines or services (such as telepharmacy, teledermatology, telepsychology and telesurgery) where these are seen as embraced within more generic terms – most usually telemedicine. Medical terms are, similarly, not included but some behaviours (relating to lifestyles) of particular relevance are. In addition, some detailed technical terms are omitted in view of the service focus of TeleSCoPE.[1] Operational aspects of the technologies are nevertheless recognised as important and defined where appropriate.

Future Actions Related to the Glossary

It is considered that the definitions offered in this document that relate to telehealth should be made widely available so that understandings regarding them are more consistently in place. This is of particular importance given the extent of attention being given to telehealth by the European Commission.

Consultation regarding this document is, in any case, taking place during the first half of 2011 with over 350 stakeholders (from a variety of sectors) within the member states of the European Union. This relates to Workpackage 4 of the TeleSCope project. Their views and opinions on definitions are being taken into account in order to amend or add to the *Glossary of Terms in Telehealth*.

Appendix: Developments and Definitions in Slovenia – Dodatek: Stanje in izrazje v Sloveniji

V kontekstu zagotavljanja zdravstvenih storitev na daljavo uporabljamo več pojmov, med katerimi so ključni "telemedicina" (angl. telemedicine), "zdravje na daljavo" (angl. telehealth) in "oskrba na daljavo" (angl. telecare). Številni drugi pojmi, povezani s tovrstnimi storitvami, so strokovni pojmi iz kliničnega okolja, npr. tele-posvetovanje, tele-dermatologija, tele-kardiologija, tele-psihiatrija ali tele-rehabilitacija. Drugi so povezani s procesi ali s postopki, npr. telemetrija, spremljanje na daljavo (angl. telemonitoring) ali obisk na daljavo (angl. tele visit). Naslednja skupina pojmov prihaja s področja informacijskih tehnologij: video konferenca, širokopasovno omrežje, medmrežje, prenos podatkov, protokol TCP/IP, USB ipd.

Tehnični in tehnološki pojmi so v slovenskem jeziku v glavnem definirani v prevodih mednarodnih in evropskih standardov, osnovne pojme, kot so telemedicina, zdravje na daljavo in oskrba na daljavo, pa je potrebno ustrezno definirati. Obstajajo številne neusklajene definicije, ki so rezultat razumevanja posameznih avtorjev znanstvenih ali strokovnih člankov, razumevanja posameznih strokovnih ali interesnih združenj ali pa strokovnih izkušenj skupin oz. posameznikov.

Evropska komisija je v svojem dokumentu o koristih telemedicine za paciente, zdravstvene sisteme in družbo[2] definirala pojem "telemedicina" kot "zagotavljanje zdravstvenih storitev z uporabo informacijskih in telekomunikacijskih tehnologij v primerih, ko izvajalec zdravstvene storitve in pacient (oziroma dva izvajalca zdravstvene storitve) nista na istem mestu. Vključuje varen prenos medicinskih podatkov in informacij v obliki besedila, zvoka, slike ali v drugi obliki, ki je potrebna za preventivo, diagnosticiranje, zdravljenje ali spremljanje pacienta".

V tem dokumentu Evropska komisija torej ni posebej opredelila pojma zdravje na daljavo, a je iz vsebine razvidno, da v okviru telemedicinskih storitev storitev dejansko govori tudi o storitvah, ki jih opredeljujemo kot zdravje na daljavo.

Evropski koordinacijski komite radiološke, elektromedicinske in zdravstvenoinformacijske industrije (COCIR) je prevzel definicijo Evropske komisije, vendar meni, da pojem vključuje področja, kot so zdravje na daljavo, oskrba na daljavo in številne medicinske telediscipline.[3] Pojem telemedicine po mnenju COCIR vključuje tako storitve kot sisteme, ki povezujejo pacienta z izvajalcem oskrbe ter pomagajo pri diagnosticiranju in spremljanju pacienta s kronično boleznijo ali upravljanju postopkov. Telemedicina po njihovem mnenju daje tudi večje opolnomočenje pacientu.

Ameriško združenje za telemedicino (ATA) je pojem telemedicina definiralo kot "izmenjavo medicinskih informacij z uporabo elektronskih komunikacijskih sredstev za izboljšanje zdravstvenega stanja pacienta".[4] Nacionalna pobuda za zdravje na daljavo iz Kanade (NIFTE) je definirala le pojem "zdravje na daljavo", pojem telemedicina pa omenja zgolj kot njenega zgodovinskega predhodnika.[5]

Oskrba na daljavo

Evropska komisija v svojem ključnem dokumentu[2] ni definirala pojma "oskrba na daljavo", čeprav govori o storitvah, ki niso strogo medicinske, pač pa posegajo na področje celostne dolgotrajne oskrbe bolnikov. Standard ETSI TR102415 definira oskrbo na daljavo kot "izvajanje (nudenje) zdravstvene in socialne oskrbe posamezniku v domačem okolju ali širši skupnosti s podporo oziroma ob uporabi informacijsko-komunikacijske tehnologije (IKT". Vključuje tudi storitve zagotavljanja varnosti in elektronske podpore tehnologije".

V evropskem projektu TeleSCopE je oskrba na daljavo (telecare) definirana kot "The means by which technologies and related services at a distance are accessed by or provided for people and/or their carers at home or in the wider community, in order to facilitate empowerment or the provision of care and/or support in relation to needs associated with their health and well-being" (tabela 3).

Slovenske definicije pojmov

V Sloveniji se je pojem telemedicina že udomačil in ga razumemo kot "medicina na daljavo". Stereotipne predstave za tovrstne storitve so npr. izvajanje kirurških operacij na daljavo, vrednotenje radioloških slik na daljavo, posvetovanja med zdravstvenimi delavci na podlagi slike, signala, zvoka itd. Pogosto naveden primer telemedicinske storitve je tudi merjenje EKG signala v domačem okolju in posredovanje signala zdravniku v klinično okolje, kjer zdravnik EKG ovrednoti in pošiljatelju (bolniku) vrne oceno, na podlagi katerega naj bi bolnik ustrezno ukrepal. Pojem "zdravje na daljavo" se pri nas še ni udomačil, saj nekateri prevajajo angleški izraz kot "tele-zdravje".

V Sloveniji načrtujemo bistvene spremembe na področju dolgotrajne oskrbe, kamor spada tudi dolgotrajna oskrba kronično bolnih oseb . Kot del te oskrbe so v okviru predloga zakona o dolgotrajni oskrbi načrtovane tudi storitve oskrbe na daljavo, ki so opredeljene kot "pomoč na daljavo", zato je v nadaljevanju definiran tudi ta pojem.

Upravni odbor Slovenskega društva za medicinsko informatiko je na svoji seji dne 24. 5.2010 pooblastil dva svoja člana, da v sodelovanju z drugimi strokovnjaki pripravita Izhodišča za nacionalno strategijo zdravja na daljavo (telehealth), ki vključuje tudi telemedicino. Ta delovna skupina se je že poenotila glede definicij pojmov telemedicina, zdravje na daljavo in oskrba na daljavo, ki so podane v nadaljevanju. Predloge definicij je posredovala Odboru za zdravstveno-informacijske standarde pri Ministrstvu za zdravje, da jih uvrstiti v (zdravstveni) Terminološki slovar.

- **Telemedicina (angl. telemedicine)**

Telemedicina je zagotavljanje zdravstvenih storitev z uporabo informacijskih in telekomunikacijskih tehnologij v primerih, ko sta izvajalec zdravstvene storitve in pacient, oziroma dva izvajalca zdravstvene storitve, prostorsko ločena.

- **Zdravje na daljavo (angl. telehealth)**

Zdravje na daljavo je zagotavljanje z zdravjem povezanih storitev na daljavo. Predstavlja razširitev pojma "telemedicina" na področji ohranjanja in izboljševanja zdravja.

- **Oskrba na daljavo (angl. telecare)**

Oskrba na daljavo je skupek različnih storitev na daljavo, ki jih izvajamo z uporabo IKT. Namenjene so bodisi neposredno osebam z zmanjšanimi zmožnostmi, bodisi njihovim oskrbovalcem, ki v domačem okolju ali širši skupnosti potrebujejo zunanjo pomoč. Z njimi izvajamo oskrbo in dajemo podporo pri obvladovanju vsakdanjih potreb in prizadevanjih za čim bolj samostojno življenje.

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Bilten SDMI ■

Poročilo o izvedbi evropske konference EFMI STC2011 (Laško, 14.-15.4.2011)

Mojca Paulin, Tomaž Marčun

Evropska federacija za medicinsko informatiko (EFMI) vsako leto skupaj z enim od nacionalnih društev organizira tematsko konferenco z angleškim nazivom Special Topic Conference. Za leto 2011 je federacija soorganizacijo konference podelila Slovenskemu društvu za medicinsko informatiko (SDMI), kar je bilo za naše društvo velika čast in obenem velika odgovornost, saj so tovrstne konference zahteven mednaroden, strokovno izobraževalni dogodek.

Priprave so se pričele pred letom dni, ko sta bila oblikovana mednarodni programski in lokalni organizacijski odbor v spodnji sestavi.

Slika 1 Predsednica in podpredsednika Programskega odbora.

Programski odbor

- Lacramioara Stoicu Tivadar, predsednik
- Bernd Blobel, podpredsednik
- Tomaž Marčun, podpredsednik
- György Surjan
- Vesna Urošević
- Mira Hercigonja Szekeres

Slika 2 Predsednica in podpredsednik Organizacijskega odbora.

Organizacijski odbor

- Mojca Paulin, predsednica
- Andrej Orel, podpredsednik
- Nina Dolenc
- Marija Zevnik
- Mojca Zima
- Danila Perhavec

V aprilu 2010 so se oba odbora in vodstvo EFMI srečali na Ptuju in dorekli potek pripravljalnih aktivnosti in programsko zasnovo konference.

V nadaljnjih mesecih je programski odbor pozval avtorje k oddaji prispevkov in poskrbel za zbiranje in recenzijo. V decembru 2010 je programski odbor izmed 41 prispelih predlogov, ki so jih poslali strokovnjaki iz 20 držav izbral 21 prispevkov, 9 posterjev in 3 delavnice ter dogovoril sodelovanje 3 vabljenih predavateljev. V januarju in februarju je nato potekalo zbiranje končnih prispevkov in priprava zbornika. V zadnjih mesecih je sledilo končno oblikovanje programa, vključno s svečanimi deli konference.

Pred konferenco so potekale tudi obsežne organizacijske priprave. Dogovorjene so bile podrobnosti z gostiteljem konference – hotelom Thermana v Laškem. Zagotovljeno je bilo sprotno obveščanje zainteresirane javnosti in promocijske aktivnosti preko spletne strani in ciljanih mednarodnih in domačih obvestil. Organizirani so bili registracijski postopki in prevozi za tuje udeležence. Dogovorjeni in organizirani so bili družabni deli konference. Zasnovane in oblikovanje so bile tudi brošure in ostala gradiva za udeležence.

Slika 3 Članice Organizacijskega odbora, ki so skrbele za registracijo udeležencev.

Z zavzetimi pripravami konference smo k udeležbi privabili preko 140 udeležencev iz večine evropskih držav in tudi širše – celo iz Japonske in ZDA. Organizacijski odbor je po tihem pričakoval še nekoliko večje število udeležencev, a so v številnih okoljih zaradi gospodarske krize varčevali pri udeležbah na mednarodnih konferencah. V primerjavi s pričakovanji je bila udeležba bistveno manjša iz držav bivše Jugoslavije.

Tema konference EFMI STC2011 je bila "**E-salus trans confinia sine finibus – e-Zdravje preko meja brez preprek**", kar se v današnjem času vse večje mobilnosti oseb in vse tesnejšega povezovanja mest, regij in držav kaže kot vse bolj pomembna usmeritev. Osrednja naloga te usmeritve je zagotoviti in upravljati čezmejno interoperabilnost sistemov za vodenje elektronskih zdravstvenih zapisov ob sprotnih spremembah številnih elementov ki so podlaga ali vplivajo na delovanje tovrstnih sistemov.

Konferenco sta svečano odprla predsednik SDMI g. Ivan Eržen in predsednik EFMI g. John Mantas. Udeležence je v imenu ministra za zdravje nagovorila ga. Mateja de Leonni Stanonik, ki je predstavila slovenske nacionalne načrte na področju eZdravja.

Slika 4 Otvoritev konference.

Strokovni vrhunci konference so bila predavanja vabljenih predavateljev. G. Rifat Latifi je predstavil dolgoletne izkušnje širjenja znanja in uvajanja telemedicine za zagotavljanje visoko kakovostnih medicinskih storitev v manj razvitih področjih. G. Bernd Blobel je podal zelo zanimivo predavanje o različnih vidikih interoperabilnosti informacijskih sistemov v zdravstvu. Ob koncu konference je g. Ferenc Bari kritično izpostavil problematiko šibke zastopanosti informacijskih vsebin v programih izobraževanja zdravstvenih delavcev in izpostavil kako nujne so te vsebine v rednem in funkcionalnem izobraževanju.

Ostali predavatelji in pripravljavci posterjev, med drugim tudi mladi raziskovalci, so izpostavili številne aktualne teme zdravstvene informatike, kot so razvoj regionalnih informacijskih sistemov in aplikacij, čezmejni projekti eZdravja, vloga pacienta v čezmejnih sistemih eZdravja, večjezični in večkulturni vidiki eZdravja, mednarodna standardizacija, zagotavljanje skladnosti sistemov eZdravja s standardi in priporočili, varnost in zaščita povezanih sistemov, elektronske komunikacije in čezmejno izobraževanje.

Program konference so popestrili slovenski predavatelji, ki so prikazali domače projekte in vzpostavljene rešitve. Med temi prispevki je bila posebej odmevna predstavitev rešitve za elektronsko svetovanje za najstnike, za katero že 10 let uspešno skrbi Zavod za zdravstveno varstvo Celje.

Ob zaključku konference so predsednik EFMI g. John Mantas in številni udeleženci izpostavili, da je bila konferenca zelo kakovostno pripravljena in odlično izpeljana, česar smo bili v programskem in organizacijskem odboru, kakor tudi v SDMI zelo veseli.

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